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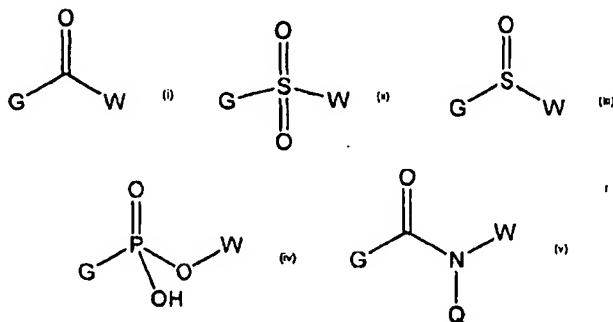
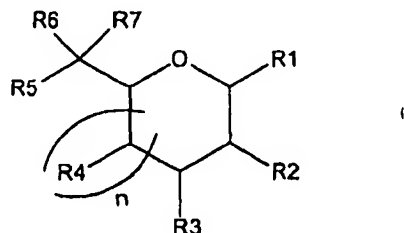
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(54) Title: ANOMERIC DERIVATIVES OF MONOSACCHARIDES



(57) Abstract: A compound of formula (I), wherein, n is 0 or 1; R6 and R7 are hydrogen, or together form a carbonyl oxygen; R1 is selected from the group consisting of hydrogen; -N(Z)Y and -C(Z)Y wherein; When R1 is -N(Z)Y, then: Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(Y)Z (i-v); Z is selected from hydrogen or X1; Q is selected from hydrogen or W; The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms, The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms, When R1 is -C(Z)Y, then: Y is selected from the group consisting of two hydrogen atoms, a double bonded oxygen (=O) to form a carbonyl, and a triple bonded nitrogen to form a nitrile. Z is absent, or is selected from hydrogen or U, Wherein U is selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aminoalkyl, aminoaryl, aryloxy, alkoxy, heteroaryloxy, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms, When R1 is H, at least two of the groups R2, R3, R4 and R5 are selected from the group consisting of -OX2 or

-N(T)Y, and the others are independently selected from hydrogen, -OH, -OX2, -N(T)Y, wherein Y is as defined above, T is selected from hydrogen or X2; and X2 is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms, When R1 is N(Z)Y or C(Z)Y, at least one of the groups R2, R3, R4 and R5 are selected from the group consisting of -OX2 or -N(T)Y, and the others are independently selected from hydrogen, -OH, -OX2, -N(T)Y, wherein Y is as defined above, T is selected from hydrogen or X2; and X2 is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms.

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## Anomeric Derivatives of Monosaccharides

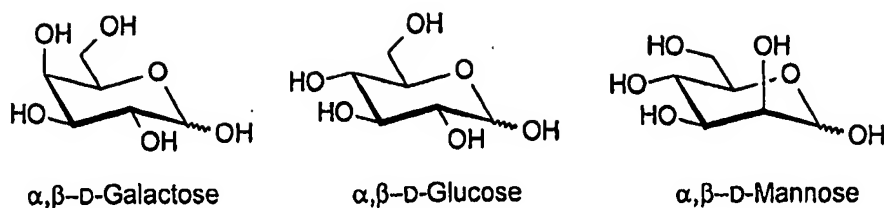
### FIELD OF THE INVENTION

5 This invention relates to methods for the preparation of combinatorial libraries of potentially biologically active mainly monosaccharide compounds. These compounds are variously functionalized, with a view to varying lipid solubility, size, function and other properties, with the particular aim of discovering novel drug or drug-like compounds, or compounds with useful properties. The  
10 invention provides intermediates, processes and synthetic strategies for the solution or solid phase synthesis of monosaccharides, variously functionalised about the sugar ring, including the addition of aromaticity and charge, and the placement of amino acid and peptide side chain units or isosteres thereof.

15

### BACKGROUND OF THE INVENTION

From a drug discovery perspective, carbohydrate pyranose and furanose rings and their derivatives are well suited as templates. Each sugar  
20 represents a three-dimensional scaffold to which a variety of substituents can be attached, usually *via* a scaffold hydroxyl group, although occasionally a scaffold carboxyl or amino group may be present for substitution. By varying the substituents, their relative position on the sugar scaffold, and the type of sugar to which the substituents are coupled, numerous highly diverse  
25 structures are obtainable. An important feature to note with carbohydrates, is that molecular diversity is achieved not only in the type of substituents, but also in the three dimensional presentation. The different stereoisomers of carbohydrates that occur naturally (examples include glucose, galactose, mannose etc, Fig 1), offer the inherent structural advantage of providing  
30 alternative presentation of substituents.

**Fig. 1**

5 The first example of a combinatorial approach employing carbohydrate chemistry, was a symposium report on the design and synthesis of a peptidomimetic using a glucose scaffold in the early 1990's<sup>1</sup>. The results, revealed that the glucose based structures designed as mimetics of a potent somatostatin (SRIF) agonist acted as agonists at low concentration, and at  
10 high concentration became the first known antagonists of SRIF. Although hardly the production of a library, the results were unique.

Continuing in part the work commenced in the early 1990's, Nicolaou and co-workers began developing carbohydrate based peptido-mimetics targeting  
15 integrins. Many integrins recognize an Arg-Gly-Asp (RGD) sequence in ligands such as fibronectin, vitronectin and fibrinogen, each binding with different affinities to the individual integrin receptors. Through a process of rational design a number of carbohydrate based RGD mimetics were synthesized. The chemical synthesis of nine different compounds by this  
20 group with very few common intermediates required a considerable amount of chemical effort. It was evident from such results, that in order to generate a number of different structures in a facile manner new chemistries needed to be developed to streamline and enable what at this stage was unfortunately a protracted and arduous methodology.

25

Since 1998 researchers in the group of Kunz<sup>2</sup> have been developing a number of carbohydrate building blocks with a similar purpose in mind. In general the building blocks that they have developed are coupled to a solid support to effect the desired chemical transformations. The chemistry  
30 developed can be employed to achieve, like the work of Hirschmann and co-



workers<sup>3</sup>, the introduction of peptidomimetic side chains to carbohydrate scaffolds in an effort to produce glyco-based mimetics of cyclic peptides. Admittedly, with the chemistry they have developed, there are inherent limitations in the types of functional groups that they are able to introduce and  
5 the range of stereoisomeric building blocks that they are able to employ.

It is now becoming reasonably established in the art that relates to the solid phase production of combinatorial carbohydrate based libraries, that one of five protecting groups on a carbohydrate scaffold is a protecting group  
10 modified as a linker, so as to allow coupling of the block to a solid support. The strategy that then follows is simple, remove a protecting group and effect coupling at the freed functionality with a peptidomimetic or other reagent. Remove another protecting group and couple with the next reagent, and so on.

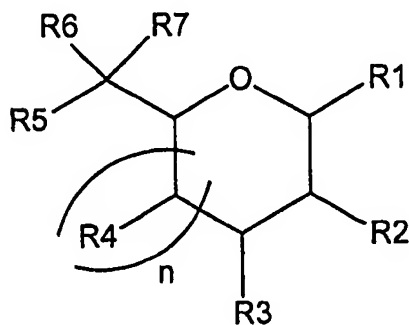
15 Following this generally accepted principle, a system has been developed that allows the chemical synthesis of highly structurally and functionally diverse derivatised carbohydrate and tetrahydropyran structures, of both natural and unnatural origin. The diversity accessible is particularly augmented by the  
20 juxtaposition of both structural and functional aspects of the molecules. In order to access a wide range of diverse structures, stereo-center inversion chemistry is required, so as to achieve non-naturally occurring and hard to get sugars in a facile manner. Other chemistries are also required that provide unnatural deoxy or deoxy amino derivative which impart greater structural  
25 stability to the drug-like target molecules. With a suite of reagents to effect a suitable range of chemistries on a solid support, allowing such things as; wide functional diversity, highly conserved intermediates, a limited number of common building block to be required, and with suitable chemistry to allow access to unusual carbohydrate stereo-representations and including access  
30 to deoxy and deoxy amino analogues, a methodology is then established that can create focused libraries for a known target, or alternatively diversity libraries for unknown targets for random screening.

- Many of the traditional methods of carbohydrate synthesis have proved to be unsuitable to a combinatorial approach, particularly because modern high-throughput synthetic systems require that procedures to be readily automatable. The compounds and processes described herein are particularly suited to the solid and solution phase combinatorial synthesis of carbohydrate-based libraries, and are amenable to automation. The methods of the invention yield common intermediates that are suitably functionalized to provide diversity in the structure of the compounds so generated. In this way the technology described can produce many and varied compounds around the basic structure shown in Figure 1. Using this method, it is possible to introduce varied functionality in order to modulate both the biological activity and pharmacological properties of the compounds generated.
- Thus the compounds and methods disclosed herein provide the ability to produce random or focused combinatorial-type libraries for the discovery of other novel drug or drug-like compounds, or compounds with other useful properties in an industrially practical manner.
- It will be clearly understood that, although a number of prior art publications are referred to herein, this reference does not constitute an admission that any of these documents forms part of the common general knowledge in the art, in Australia or in any other country.

SUMMARY OF THE INVENTION

In a first aspect, the invention provides a compound of formula I

5



formula I

Wherein,

n is 0 or 1; the ring may be of any configuration and the anomeric center may be of either the  $\alpha$  or  $\beta$  configuration;

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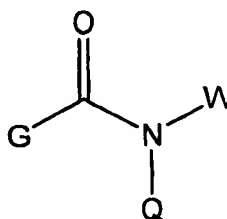
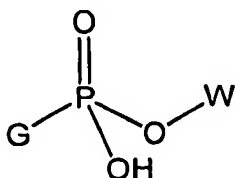
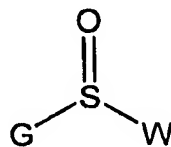
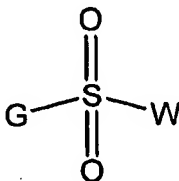
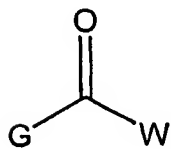
R6 and R7 are hydrogen, or together form a carbonyl oxygen;

R1 is selected from the group consisting of hydrogen;  $-N(Z)Y$  and  $-C(Z)Y$  wherein;

15

When R1 is  $-N(Z)Y$ , then:

Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in  $N(Y)Z$ ;



Z is selected from hydrogen or X1;

Q is selected from hydrogen or W;

5       The groups W are independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms which is optionally substituted, branched and/or linear. Typical substituents include but are not limited to OH, NO, NO<sub>2</sub>, NH<sub>2</sub>, N<sub>3</sub>, halogen, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate, phosphoramidate, hydrazide, hydroxamate, hydroxamic acid;

15       The groups X1 are independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms which is optionally substituted, branched and/or linear. Typical substituents include but are not limited to OH, NO, NO<sub>2</sub>, NH<sub>2</sub>, N<sub>3</sub>, halogen, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate, phosphoramidate, hydrazide, hydroxamate, hydroxamic acid;

25       When R1 is -C(Z)Y, then:

Y is selected from hydrogen, double bond oxygen (=O) to form a carbonyl, or triple bond nitrogen to form a nitrile.

Z may be optionally absent, or is selected from hydrogen or U,

Wherein U is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aminoalkyl, aminoaryl, aryloxy, alkoxy, heteroaryloxy, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms which is optionally substituted, branched and/or linear. Typical substituents

include but are not limited to OH, NO, NO<sub>2</sub>, NH<sub>2</sub>, N<sub>3</sub>, halogen, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate, phosphoramidate, hydrazide, hydroxamate, hydroxamic acid, heteroaryloxy, aminoalkyl, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, which may optionally be further substituted.

10 Suitably, When R<sub>1</sub> is H, at least two of the groups R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are selected from the group consisting of -OX<sub>2</sub> or -N(T)Y, and the others are independently selected from hydrogen, -OH, -OX<sub>2</sub>, -N(T)Y, wherein Y is as defined above, T is selected from hydrogen or X<sub>2</sub>; and X<sub>2</sub> is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or  
15 heteroarylalkyl of 1 to 20 atoms,

When R<sub>1</sub> is N(Z)Y or C(Z)Y, at least one of the groups R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are selected from the group consisting of -OX<sub>2</sub> or -N(T)Y, and the others are independently selected from hydrogen, -OH, -OX<sub>2</sub>, -N(T)Y,  
20 wherein Y is as defined above, T is selected from hydrogen or X<sub>2</sub>; and X<sub>2</sub> is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,

It is understood that the rules of molecular stoichiometry will be upheld  
25 by the default addition of hydrogens atoms as required.

The groups Z and Y may be combined to form a monocyclic or bicyclic ring structure of 4 to 10 atoms. This ring structure may be further substituted with X groups;

30

The groups R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are independently selected from hydrogen, OH, , NHDde, NHDTPM and other vinylogous amines, N(Z)Y, wherein N(Z)Y is as defined above, OX and X is independently selected from

alkyl, alkenyl, alkynyl, heteroalkyl, aminoalkyl, aminoaryl, aryloxy, alkoxy, heteroaryloxy, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms which is optionally substituted, branched and/or linear. Typical  
5 substituents include but are not limited to OH, NO, NO<sub>2</sub>, NH<sub>2</sub>, N<sub>3</sub>, halogen, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate,  
10 phosphoramidate, hydrazide, hydroxamate, hydroxamic acid;

With the proviso that when R<sub>2</sub> is N(Z)Y, R<sub>6</sub> and R<sub>7</sub> are hydrogen, and R<sub>4</sub> and R<sub>5</sub> are OH or together form a benzylidene or substituted benzylidene, then R<sub>1</sub> cannot be N(Z)Y.

15

A preferred embodiment of the first aspect provides for compounds of formula I in which R<sub>1</sub> is H and R<sub>4</sub> is N(Z)Y;

In a particularly preferred embodiment R<sub>1</sub> is H and R<sub>4</sub> is N(Z)Y wherein Z is  
20 hydrogen;

A further embodiment of the first aspect provides for compounds of formula I in which R<sub>1</sub> and R<sub>4</sub> are independently N(Z)Y;

25 Another embodiment provides for compounds of formula I in which R<sub>1</sub> is H and both R<sub>2</sub> and R<sub>4</sub> are N(Z)Y;

In a preferred embodiment provides for compounds of formula I in which the ring is of the gluco, galacto or allo configuration;

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A further embodiment provides for compounds of formula I in which R<sub>1</sub> is N(Z)Y and R<sub>2</sub> is N(Z)Y;

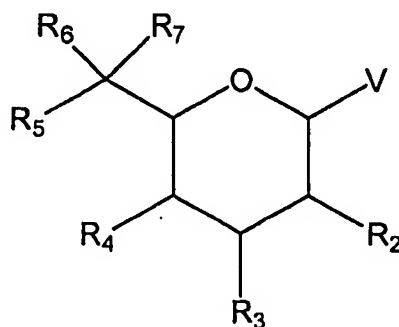
A further embodiment provides for compounds of formula I in which R1 is P(Z)Y and R2 is N(Z)Y, wherein P is carbon and Y is hydrogen.

A further embodiment provides for compounds of formula I in which R1 is P(Z)Y and R4 is N(Z)Y, wherein P is carbon and Y is hydrogen.

A further embodiment provides for compounds of formula I in which R1 is N(Z)Y and R5 is N(Z)Y and the ring is of the furan form.

10 In a second aspect, the invention provides for a method of synthesis of compounds of formula I in which R1 is hydrogen, comprising the step of reducing a synthetic intermediate of formula II, in which the substituent V is either bromine or chlorine, R6 and R7 are as defined in the first aspect, R5, R4, R3, and R2 are independently selected from OH, O-acyl, N<sub>3</sub>, NHDde, NHDTPM, NHZ, NHBoc, phthalimide, O-protecting group or when R6 and R7 together for a carbonyl oxygen, R5 may additionally be optionally substituted O-alkyl, O-arylalkyl or O-aryl. Where the protecting groups may be chosen from any suitable oxygen protecting groups known in the art, including acetals and ketals which protect two adjacent oxygens.

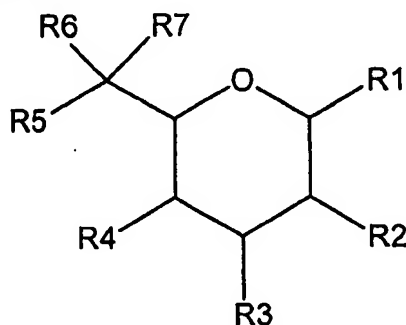
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formula II

In a third aspect, the invention provides for a method of synthesis of compounds of formula I in which R1 is N(Z)Y comprising the step of reacting a compound of formula II with an azide nucleophile, in which the substituents for formula II are as described in the second aspect.

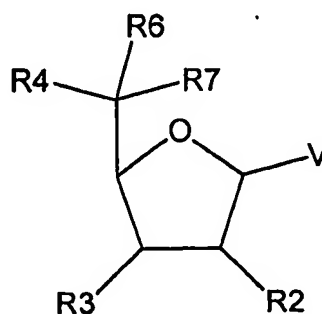
In a fourth aspect, the invention provides for a method of combinatorial synthesis of compounds of the formula I comprising the step of immobilizing a compound of formula III onto a support. Said support may be soluble or insoluble. Non-limiting examples of insoluble supports include derivatised polystyrene, tentagel, wang resin, MBHA resin, aminomethylpolystyrene, rink amide resin etc. Non-limiting examples of soluble supports include DOX-mpeg, polyethylene glycol etc.



formula III

Wherein R1 is as defined in the first aspect, R2, R3, R4, R5, R6 and R7 are as defined in the second aspect, and the linkage between the compound of formula III and the support is through any of positions R2, R3, R4 or R5.

In a fifth aspect, the invention provides for a method of synthesis of compounds of formula I in which R1 is N(Z)Y, comprising the step of reacting a compound of formula IV in the presence of a lewis acid with an azide source.



formula IV

in which the substituent V is -OAcyl, R6 and R7 are as defined in the first

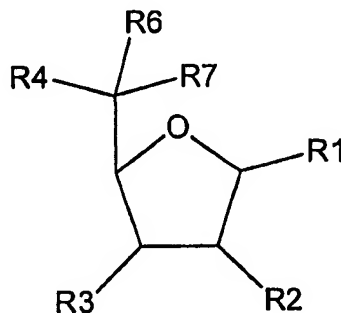


aspect, R4, R3, and R2 are independently selected from OH, O-acyl, N<sub>3</sub>, NHDde, NHDTPM, NHZ, NHBOC, phthalimide, O-protecting group or when R6 and R7 together for a carbonyl oxygen, R4 may additionally be optionally substituted O-alkyl, O-arylalkyl or O-aryl. Where the protecting groups may be  
5 chosen from any suitable oxygen protecting groups known in the art, including acetals and ketals which protect two adjacent oxygens.

In a sixth aspect, the invention provides for a method of synthesis of compounds of formula I in which R1 is H, comprising the step of reducing a  
10 compound of formula IV in which the substituents for formula II are as described in the fifth aspect.

In a seventh aspect, the invention provides for a method of combinatorial synthesis of compounds of formula I comprising the step of immobilizing a  
15 compound of formula V onto an support. Said support may be soluble or insoluble. Non-limiting examples of insoluble supports include derivatised polystyrene, tentagel, wang resin, MBHA resin, aminomethylpolystyrene, rink amide resin etc., Non-limiting examples of soluble supports include DOX-mpeg, polyethylene glycol etc.

20



formula V

Wherein R1 is as defined in the first aspect, R2, R3, R4, R6 and R7 are as defined in the fifth aspect, and the linkage between the compound of formula  
25 V and the support is through any of positions R2, R3, or R4.

In a eighth aspect, the invention provides for a method of solution phase combinatorial synthesis of compounds of formula I comprising the step of alkylating a free hydroxyl on a compound of formula III, wherein R1 is as defined in the first aspect, R2, R3, R4, R5, R6 and R7 are as defined in the  
5 second aspect and any one of the protecting substituents may be removed prior to alkylation.

Compounds of the invention are useful in screening for biological activity.

10 For the purposes of this specification it will be clearly understood that the word "comprising" means "including but not limited to", and that the word "comprises" has a corresponding meaning.

General Solution and Solid Phase Methods For Examples 1-21

5 General Method 1: Formation of a Glycosyl Bromide

To a solution of the anomeric-acetate compound (100 mmol) in dichloromethane (250 mL) at 0°C, was added a solution of 33% HBr in acetic acid (100mL). The solution was then stirred for 2 h at room temperature. At this time chloroform was added to the suspension and the resulting solution  
10 poured onto ice/water. The chloroform layer was then collected and washed with cold water, saturated sodium hydrogen carbonate, brine, dried (MgSO<sub>4</sub>), and the solvent removed to leave a foam. This foam was trituated with ether (50 mL) for 30 min and the resulting solid filtered to give the glycosyl bromide as a white solid. Yield typically greater than 95%.

15

General Method 2: Reduction at the Anomeric Centre to Form a Glycitol

To a suspension of glycosyl bromide (100 mmol) in dry toluene 200 mL was added tributyltin hydride (110 mmol) and the whole refluxed under nitrogen for 3 h. The suspension was concentrated to dryness and the residue re-  
20 dissolved in a 2:1 dichloromethane/chloroform (250 mL) mixture. To the residue was then added potassium fluoride (20 g) in water (100 mL), and the heterogeneous solution stirred vigorously for 45 min. The resulting suspension was filtered through a pad of celite and washed several times with dichloromethane. The combined filtrates were then washed with water, brine,  
25 dried (MgSO<sub>4</sub>), and solvent removed in vacuo to leave a solid in typically quantitative yield.

General Method 3: Solution Phase Zemplen

To a suspension of the acetylated compound (100 mmol) in dry methanol  
30 (125 mL) at 0°C was added a solution of sodium methoxide (0.33 mmol) in dry methanol (125 mL) and the mixture was stirred under nitrogen for 2 h. Amberlite IR 120 H<sup>+</sup> was added until pH 5 was reached, the solution was filtered and the resin washed several times with a 2:1

methanol/dichloromethane mixture. The combined filtrates were then concentrated to dryness to leave a solid. Typically quantitative yield.

#### General Method 4: Solution Phase Benzylidene Protection

- 5 To a solution of the triol (~100 mmol) in dry *N,N*-dimethylformamide (325 mL)/acetonitrile (200 mL) was added 4-methoxybenzaldehyde dimethyl acetal (180 mmol) and *p*-toluene sulfonic acid (2.5 mmol). This solution was then heated at 60°C on a rotary evaporator at 300 mmHg for 30 min and then over the course of 4 h the pressure was reduced to 80 mmHg and approximately
- 10 200 mL of solvent collected. After this time a second batch of reagent (70 mmol) and acetonitrile (125 mL) was added and the evaporation process repeated over 2 h. All solvent was then removed under reduced pressure and the residue re-dissolved in an 8:1 chloroform/triethylamine mixture, washed with dilute sodium hydrogen carbonate, dried ( $\text{MgSO}_4$ ) and the
- 15 solvent removed under reduced pressure to leave a oil. The oil was typically loaded onto a pad of silica and eluted with ~10% ethyl acetate in light petroleum (40-60°C), to provide a white solid.

#### General Method 5: Solution Phase Benzoylation

- 20 The sugar (100 mmol) was partially suspended in pyridine (400 mL) and *p*-chlorobenzoyl chloride (46 mL, 120 mmol) added dropwise at 0°C and the resulting reaction mixture stirred at room temperature for 2 h. After this time cold water (30 mL) was added and the solution stirred for a further 1 h at room temperature. All solvents were then removed under reduced pressure
- 25 and any traces of pyridine azeotropically removed with toluene. The residue solid was then redissolved in chloroform and washed with water, 10% citric acid, saturated sodium hydrogen carbonate, brine, dried ( $\text{MgSO}_4$ ) and concentrated under reduced pressure to leave a foam. This foam was triturated with ether and the resulting solid filtered to give the benzoylated
- 30 compound as a solid, typical yield ~85%.

#### General Method 6: Solution Phase Nucleophilic Inversion of a Carbon Centre

To a solution of the sugar (100.0 mmol) in dry chloroform (300 mL) cooled to

-20°C, was added pyridine (180.0 mmol) and trifluoromethane sulfonic anhydride (115 mmol) and the whole stirred for 1 h at this temperature. The reaction was then diluted with chloroform, and the resulting solution washed with cold water, cold 10% hydrochloric acid, cold water, dried (MgSO<sub>4</sub>), and the solvent removed in vacuo. The resulting residue was then redissolved in *N,N*-dimethylformamide (600 mL), and sodium azide (500 mmol) was added at 0°C in portions. The suspension stirred overnight at room temperature. The reaction was diluted with chloroform and the resulting solution then washed with water, 10% citric acid, saturated sodium hydrogen carbonate, brine, dried (MgSO<sub>4</sub>), and the solvent removed in vacuo, followed by azeotropeing with toluene to leave the product, typically 95% yield.

#### General Method 7: Solution Phase Alkylation

To a suspension of sodium hydride (100 mmol) in dry *N,N*-dimethylformamide (360 mL) at 0°C under nitrogen was added a solution of the sugar (63.2 mmol) in dry *N,N*-dimethylformamide (30 mL). The mixture was stirred at 0°C for 15 min and then warmed to room temperature and stirred for a further 30 min. The suspension was again cooled to 0°C, the alkylating agent (85 mmol) added dropwise over a period of 5 min, after which the suspension was warmed to room temperature and stirred for 16 h. The suspension was then cooled to 0°C and the reaction quenched with ammonium chloride solution, chloroform added, and the organic layer washed with saturated sodium hydrogen carbonate, water, dried (MgSO<sub>4</sub>) and all solvent removed to leave an oil. Crude products were purified by column chromatography (typically: silica, 50% ethyl acetate in light petroleum (40-60°C)) to give the desired product as a solid, in yields of 55-95%.

#### General Method 8: Solution Phase DTPM Removal

To a solution of the DTPM derivatised sugar (100 mmol) in a 3:1 mixture of dry methanol/*N,N*-dimethylformamide (500 mL), was added hydrazine monohydrate (350 mmol) and the mixture stirred for 3 h. After this time the mixture was filtered and the filtrate was then concentrated under reduced pressure. The residue was redissolved in dichloromethane, washed with

saturated sodium chloride, dried ( $\text{MgSO}_4$ ) and all solvent removed under reduced pressure to leave a solid, typically in quantitative yield.

#### General Method 9: Solution Phase HBTU Coupling

- 5 To a solution of the acylating agent (10 mmol) and HBTU (12 mmol) in dry *N,N*-dimethylformamide (60 mL) was added diisopropylethylamine (25 mmol) and the mixture stirred for 10 min. A solution of the sugar building block (9.4 mmol) in dry *N,N*-dimethylformamide (8 mL), was then added and the mixture further stirred for 16 h. Chloroform was then added and the reaction
- 10 mixture was washed with water, 10% citric acid, saturated sodium hydrogen carbonate, brine, dried ( $\text{MgSO}_4$ ) and the solvent removed under reduced pressure to leave an oil. Purification of the products was by column chromatography (typically, silica; 50% ethyl acetate in light petroleum (40-60°C)), or alternatively by trituration with diethyl ether to give clean products in
- 15 typical yields of 55-85%.

#### General Method 10: Solution Phase Reaction with an Isocyanate

- To a solution of the sugar derivative (10 mmol) in dry dichloromethane (100 mL) was added dropwise ethyl isocyanatoacetate (10.7 mmol). The resulting
- 20 solution stirred for 3 h. In the case of a precipitate occurring, the solid was filtered after 3 h and washed with dichloromethane to give a white solid. Alternatively if no precipitate formed, chloroform was added and the reaction mixture washed with water, dried ( $\text{MgSO}_4$ ) and the solvent removed in vacuo to typically leave an oil. Purification of oils was achieved by column
- 25 chromatography. Products were typically formed in yields of 65-90%.

#### General Method 11: Solution Phase Reaction with an Anhydride

- To a solution of the sugar derivative (10 mmol) in dry dichloromethane (90 mL) was added dropwise acetic anhydride (11 mmol). The resulting solution
- 30 stirred for 16 h. In the case of a precipitate occurring, the solid was filtered after and washed with dichloromethane to yield a white solid. Alternatively if no precipitate occurred, chloroform was added and reaction mixture washed with water, 10% citric acid, saturated sodium hydrogen carbonate, brine, dried

(MgSO<sub>4</sub>) and the solvent removed under reduced pressure to leave an oil. Oils were purified by column chromatography. Products were typically formed in yields of 50-99%.

5    General Method 12: Solution Phase Reaction with an Acid Chloride

To a solution of the sugar derivative (10 mmol) in dichloromethane (100 mL) was added diisopropylethylamine (12 mmol) and an acid chloride (11.6 mmol), and the solution then stirred for 16 h. Chloroform was then added and the reaction mixture washed with water, 10% citric acid, saturated sodium  
10    hydrogen carbonate, brine, dried (MgSO<sub>4</sub>) and the solvent removed under reduced pressure to give an oil. Purification was by either column chromatography (typically: silica; 50% ethyl acetate in light petroleum (40-60°C)), or by tritiation with diethyl ether. Products were typically formed in yields of 70-80%.

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General Method 13: Solution Phase Reduction of an Azide

To a stirred solution of the sugar derivative (10 mmol) in methanol (90 mL) was a solution of ammonium chloride (50 mmol) in water (18 mL). Added to the reaction mixture was zinc dust (300 mmol) and the resulting suspension  
20    stirred for 3 h. The reaction mixture was then filtered through a pad of celite and washed with ethyl acetate. The organic layer was then collected, washed with saturated sodium hydrogen carbonate, dried (MgSO<sub>4</sub>) and all solvent removed under reduced pressure to leave a white solid. Products were typically formed in yields of 60-75%.

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General Method 14: Solution Phase Removal of p-Methoxybenzyl Group

Sugar derivative (~2mmol) was dissolved in a solution of 70% chloroform, 20% trifluoroacetic acid, 5% anisole, 5% water, and the resulting reaction mixture stirred for 6 h. All solvent was then removed under reduced pressure  
30    to leave a dark oil. Products were purified by HPLC-MS

General Method 15: Solution Phase Base Catalysed Hydrolysis

Sugar derivative (~2 mmol) was dissolved in methanol (~1.5 mL). To this

solution was 1M sodium hydroxide (0.42 mL) and the resulting reaction mixture agitated for 16h. Amberlite resin (400 mg) was added, the suspension was then stirred for 30sec, filtered, and resin washed with methanol. The resulting solutions were collected and freeze dried, and the residues then purified by HPLC-MS.

#### General Method 16: Simultaneous Removal of Benzoate and DTPM

Sugar derivative (1 mmol) was stirred at room temperature in a 1 molar NaOH/methanol solution (6 mL, 1.5 mmol) in DMF (1.5 ml) until complete consumption for (12 hrs). Hydrazine monohydrate (0.3 ml) was added and the stirring continue for 2hr. The volatile solvents were removed in vacuo and the residue was taken up in EtOAc and washed with saturated bicarbonate solution, dried over  $\text{MgSO}_4$ , and evaporated to dryness. Products were typically formed in yields of 85-90%.

#### General Method 17: Solution Phase Diazotransfer

To a solution of the sugar derivative (1 mmol) and  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  (0.02 mmol) in methanol/water (5:1, 10 mL), was added drop-wise the  $\text{TfN}_3$  solution (~4.5 mmol). The reaction mixture was stirred at room temperature for 20hr and more  $\text{TfN}_3$  (~1.4 mmol) was added. After additional 16hr, concentrated  $\text{NH}_4\text{OH}$  solution was added to quench excess  $\text{TfN}_3$  and the stirring continued for 72hr. The phases were separated and the aqueous phase was extracted with dichloromethane. The combined organic layers were washed with saturated bicarbonate solution, dried over  $\text{MgSO}_4$  and evaporated to dryness. The residue was evaporated to afford the desired product in quantitative yield.

#### General Method 18: Solution Phase Benzylidene Removal

To a solution of the sugar derivative (1 mmol) in acetonitrile/methanol/water (1:1:0.1), was added  $\text{TsOH} \cdot \text{H}_2\text{O}$  (~100micromol). The resulting reaction mixture was stirred at 50°C for 1.5 hrs. The volatile solvents were then removed in vacuo and the residue purified by flash chromatography. The desired product was typically obtained in 70-80% yield..



General Method 19: Solution Phase Silyl Protection.

To a solution of the sugar derivative (1 mmol) in pyridine (1ml), was added DMAP (1 mmol) and TBDPSCI (1.5 mmol). The resulting reaction mixture was stirred at 120°C for 45min, then the solvent removed in vacuo. The residue  
5 was taken up in dichloromethane washed with 1N HCl solution, dried over MgSO<sub>4</sub> and evaporated to dryness. The residue was chromatographed to afford the desired product in typically 85-95% yield.

General Method 20: Coupling of Building Block to Resin

10 The Trichloroacetimidate derivatised resin (IRORI Wang resin ~1 mmol) was weighed into the reaction vessel and washed with THF. The derivatised building block (1.86 mmol) was dissolved in anhydrous DCM (1.2ml), added to the resin and shaken for 3 mins. BF<sub>3</sub>·Et<sub>2</sub>O (~100μl) was added and the reaction vessel shaken continuously for 10 mins. The reaction mixture was  
15 filtered under vacuum and the resin washed with THF, DCM, and dried.

General Method 21: Solid Phase Debenzoylation

The resin bound sugar was shaken in a solution of THF/MeOH (5:1) and NaOMe (0.02 Molar) overnight. The reaction was drained and washed with  
20 anhydrous THF and repeated as described above. The reaction solvent was drained and the resin washed with THF, a solution of THF: CH<sub>3</sub>COOH: MeOH 8:1:1, THF, and DCM. The resin was dried overnight.

General Method 22: Solid Phase Alkylation

25 The resin was reacted with a 0.25 molar solution of *tert*-butoxide in DMF (5 min) and then the alkylating agent, (0.25 molar in DMF, 20 min) was reacted with the resin. The resin was washed with DMF and again treated with the two solutions, this procedure was repeated a further four times. The final wash of the resin was performed as above; with DMF, THF/MeOH/ CH<sub>3</sub>CO<sub>2</sub>H  
30 (8:1:1), THF, DCM and MeOH. The resin was then dried overnight.

General Method 23: Solid Phase Silyl Deprotection

A solution of PSHF (proton sponge hydrogen fluoride) (0.5 Molar in

DMF/Acetic Acid, 95:5) was prepared. The resin was added to the solution and the reaction was stirred at 65°C for 24 hours. The resin was then washed with DMF, MeOH/CH<sub>3</sub>COOH/THF, 1:1:8, THF and DCM, and then dried under high vacuum

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#### General Method 24: Solid Phase Azide Reduction

Resin was placed in a round bottom flask. A solution of *tert*-Butoxide (0.2 molar) in anhydrous DMF was prepared. DTT (0.2 molar) was added to the *tert*-Butoxide solution and stirring continued until all DTT dissolved. The solution was poured into the Buchner flask containing the Kans. The reactor was degassed by applying vacuum (15 mbar) and filled with nitrogen. This technique was repeated twice and the reactor shaken at room temperature for 6 hr, allowing the evolved N<sub>2</sub> gas to escape. The reaction solvent was removed from the flask and the Kans washed with DMF, THF, and MeOH before being dried under high vacuum for 12 hours.

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#### General Method 25: Solid Phase N-Acylation

##### *Method 1*

Acids were weighed into round bottom flask and DIC (diisopropylcarbodiimide) (0.25 molar) in DMF was added to make a 0.5 molar solution of the acid. The resultant solution was stirred at room temperature for 1 hour and DMAP (to 0.05 molar) was added. The solution was poured into a reactor containing the Kans and shaken vigorously. The reactor was degassed by applying vacuum (15 mbar) and filled with nitrogen. This technique was repeated twice and the reactor shaken at room temperature over night. The reaction solvent was removed from the flask and the Kans washed with DMF, MeOH, THF, MeOH, DCM and MeOH.

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##### *Method 2:*

Acids were weighed into round bottom flask and DMF was added to make a 0.5 M solution, followed by addition of DIPEA (to make 0.5 M). The solution was stirred until homogeneous and HBTU (to make 0.5 M) was added. Stirring was continued for additional 30 minutes and the solution was poured

30

into a reactor containing the Kans and shaken vigorously. The reactor was degassed by applying vacuum (15 mbar) and filled with nitrogen. This technique was repeated twice and the reactor shaken at room temperature for overnight. The reaction solvent was removed from the flask and the Kans  
5 washed with DMF, MeOH, THF, MeOH, DCM and MeOH.

#### General Method 26: Solid Phase Nitro Group Reduction

A solution of tin(II) chloride (1 Molar) in a mixture of DMF and water was prepared, filtered, the solution was poured into a reactor containing the Kans  
10 and shaken vigorously. The reactor was degassed by applying vacuum (15 mbar) and filled with nitrogen. This technique was repeated twice and the reactor shaken at room temperature for 24 hour. The Kans were washed with DMF, THF, DCM, MeOH and DCM and dried under high vacuum.

#### General Method 27: Solid Phase Fmoc Removal

A 20% v/v solution of piperidine in DMF was prepared and the solution was poured into a reactor containing the Kans and shaken vigorously. The reactor was degassed by applying a vacuum (15 mbar) and then was filled with nitrogen. This technique was repeated twice and the reactor shaken at room  
20 temperature for one hours. After one hour the solvent was removed, the Kans were washed with DMF and the deprotection was repeated as above. The reaction solvent was removed, the Kans washed with DMF, MeOH, THF, MeOH, DCM and MeOH and dried under high vacuum.

#### General Method 28: Solid Phase Guanylation

A solution of 3,5-dimethylpyrazolyl formamidinium nitrate (0.2 molar) in anhydrous DMF was prepared, and DIPEA (to 1 molar) added. The resin in Kans were pooled, added to the solution, and the reaction was stirred at 65°C for 24 hours. The reaction solvent was removed from the flask via a vacuum  
30 line and the flask shaken to release further solvent from the Kans. The Kans were washed with DMF, THF and DCM and dried under high vacuum.

#### General Method 29: Cleavage from Resin

Cleaving solutions were prepared from DCM (60%), triethylsilane (20%), TFA (20%). The Kans were opened and the resins poured into reactors in the MiniBlock, 0.7 ml of the above cleaving solution was added to each reactor and the reactors were shaken at room temperature for 3 hours. The solutions  
5 were collected into test tubes (12x75mm). The resins were washed with DCM. The washings were combined with the cleavage in the test tubes and the volatile solvents were removed by beta RVC. The residues were dried in the vacuum oven for 48 hours. Analytical samples were obtained by washing the remaining resins with acetonitrile (0.5ml), collected in 96-wells plate and  
10 evaporated in alpha RVC. The samples were re-dissolved in acetonitrile and analysed.

#### General Method 30: DTPM Protection of an Amine

To a stirred solution of the amino compound (20 mmol) dissolved in MeOH (150mL) at room temperature was added a solution of DTPM reagent (20  
15 mmol) in MeOH (50mL). After 10 min the product started to crystallise and after 40mins the reaction mixture was filtered. The crystalline residue was washed with ether and dried under vacuum to yield the DTPM protected product in typically 90% yield.

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#### General Method 31: N-Acyl formation using Diisopropylcarbodiimide

A solution of the starting material (0.62mmol) in dry DCM was added to a solution of the acid (0.76mmol) and DIC (0.76mmol) in DCM (5 mL). The reaction was stirred for 3h and the reaction mixture then diluted with DCM.  
25 The reaction mixture was washed with 10% citric acid, satd. sodium bicarbonate solution, filtered over cotton and the solvents evaporated. Column chromatography of the resulting residue provided the product, typically in 90% to near quantitative yields.

#### General Method 32: Solid Phase Cleavage of the DTPM Protecting Group.

30 A 5% solution of hydrazine hydrate in DMF was prepared. The cleavage solution was added to resin in a reactor (approx. 1 mL per 100mg of resin) and left to react for four hours. The resin was filtered, and washed with DMF,

MeOH, THF, MeOH, DCM and MeOH and then dried under high vacuum.

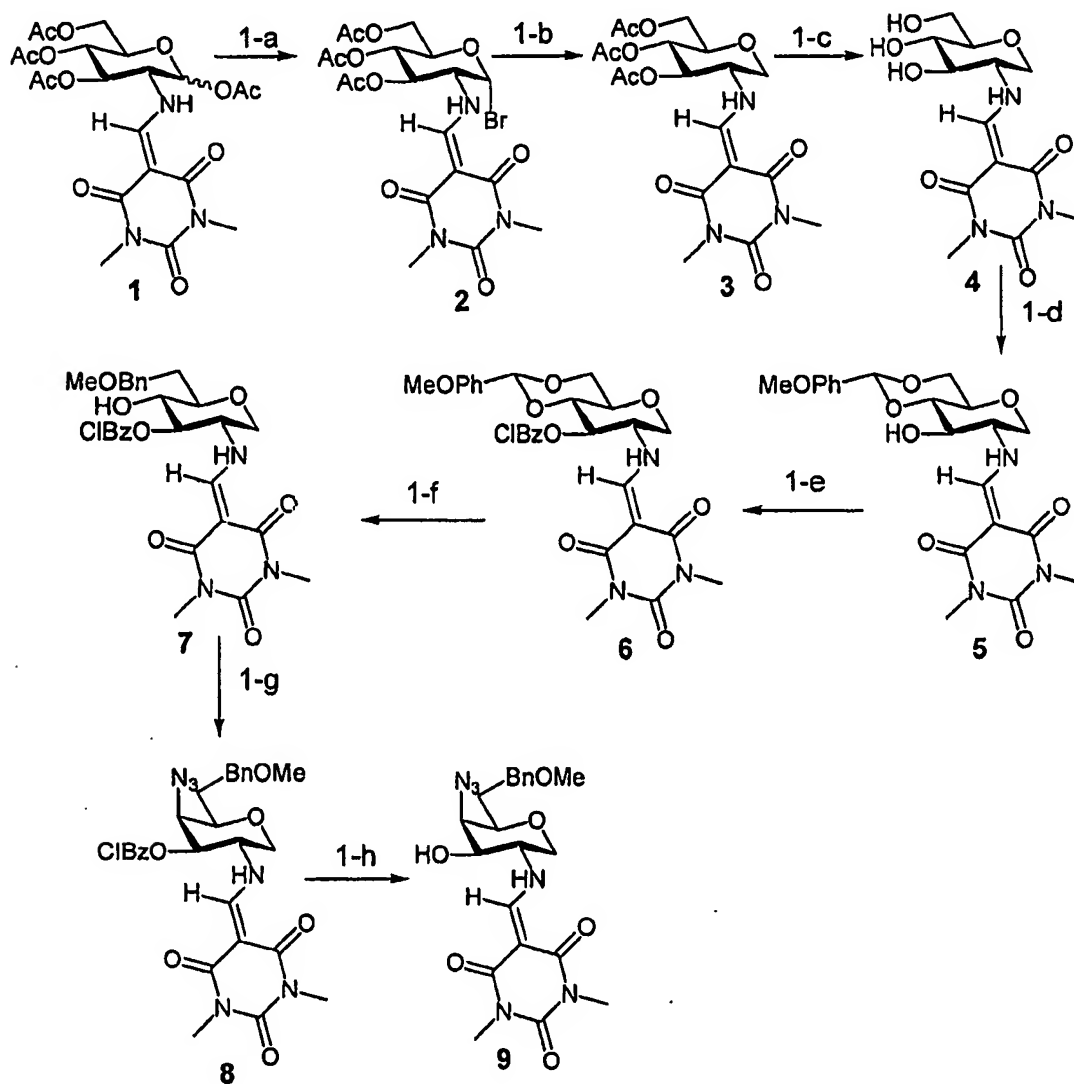
General Method 33: Selective Benzylidene Ring Opening to the 6-Position.

The benzylidene protected compound (50 mmol) was dissolved in dry *N, N*-dimethylformamide (400 mL) and added to a flask containing pre-activated 3A molecular sieves (120 g). To this suspension was added sodium cyanoborohydride (300 mmol) and the resulting reaction mixture stirred for 30 min under nitrogen. The suspension was then cooled to 0°C, and a solution of TFA (650 mmol) in dry *N,N*-dimethylformamide (80 mL) added in portions, and the suspension then heated at 55°C for 16 h. The suspension was then filtered through a bed of celite and washed several times with chloroform. These combined washings were then washed with water, 10% citric acid, saturated sodium hydrogen carbonate, brine, dried (MgSO<sub>4</sub>), and the solvent removed in vacuo to leave a yellow foam, which was azeotropically dried with toluene. Typical yields were in the order of 85-95%.

General Method 34: Formation of a Glycosyl Azide.

From the anomeric acetate derivative the glycosyl bromide was prepared as described in General Method 1. To a solution of the bromosugar (50 mmol) in acetonitrile (200 mL) was added TMS-azide (100 mmol) followed by TBAF (100 mmol). The reaction mixture was left to stir for 2 hours at which time the solvent was removed in vacuo, the residue taken up in chloroform, and the resulting solution washed with saturated sodium hydrogen carbonate, brine, dried (MgSO<sub>4</sub>), and the solvent removed in vacuo to leave a solid, typically in 85-95% yield.

Example 1: Synthesis of 1,5-anhydro-4-azido-3-O-(4-chlorobenzoyl)-2,4-dideoxy-2-[(1,3-dimethyl-2,4,6- (1H, 3H, 5H)-trioxypyrimidin-5-ylidene) methylamino]-6-O-(4-methoxybenzyl)-D-galactitol.



1-a. Synthesis of 2-deoxy-2-[(1,3-dimethyl-2,4,6- (1H, 3H, 5H)-trioxypyrimidin-5-ylidene) methylamino]-3,4,6-O-triacetyl- $\alpha$ -D-glucopyranosyl bromide (2).

- 10 Compound 2 was synthesized according to the procedure described in General Method 1. Compound 2, (96%) as a white solid.  $R_f$  (product)  $\approx$  0.75 in ethyl acetate;  $\delta_H$  (400 MHz;  $CDCl_3$ ) 2.00 (3 H, s), 2.05 (3 H, s), 2.09 (3 H, s), 3.29 (3 H, s), 3.30 (3 H, s), 3.78 (1 H, dt,  $J$  9.9 Hz and  $J$  3.6 Hz), 4.13 (1 H, dd,  $J$  13.4 Hz and  $J$  3.0 Hz), 4.35 (2 H, m), 5.19 (1 H, t,  $J$  9.8 Hz), 5.46 (1 H, t,

*J* 9.8 Hz), 6.50 (1 H, d, *J* 4.0 Hz), 8.13 (1 H, d, *J* 13.6 Hz) and 10.30 (1 H, br t, *J* 11.6 Hz); LCMS [M+H]<sup>+</sup>=534.

5 1-b. Synthesis of 1,5-anhydro-2-deoxy-2-[(1,3-dimethyl-2,4,6- (1H, 3H, 5H)-trioxypyrimidin-5-ylidene) methylamino]-3,4,6-O-triacetyl-D-glucitol (3).

Compound **3** was synthesized according to the procedure described in General Method 2. Compound **3**, quantitative yield; *R<sub>f</sub>* (product)  $\approx$  0.65 in ethyl acetate.,  $\delta_{\text{H}}$  (400 MHz; CDCl<sub>3</sub>) 2.03 (3 H, s), 2.04 (3 H, s), 2.09 (3 H, s), 3.28 (3 H, s), 3.30 (3 H, s), 3.53 (1 H, t, *J* 11.2 Hz), 3.68 (2 H, m), 4.14 (2 H, m), 4.25 (1 H, dd, *J* 12.6 Hz and *J* 5.0 Hz), 5.04 (1 H, t, *J* 9.4 Hz), 5.16 (1 H, t, *J* 9.6 Hz), 8.13 (1 H, d, *J* 13.6 Hz) and 10.10 (1 H, br t, *J* 11.4 Hz);  $\delta_{\text{C}}$  (400 MHz; CDCl<sub>3</sub>) 21.04 (CH<sub>3</sub>  $\times$  2), 21.17 (CH<sub>3</sub>), 27.63 (CH<sub>3</sub>), 28.33 (CH<sub>3</sub>), 60.36 (CH), 62.32 (CH<sub>3</sub>), 68.29 (CH), 68.62 (CH<sub>2</sub>), 73.98 (CH), 76.97 (CH), 92.65 (C), 151.97 (C), 158.84 (CH), 162.65 (C), 164.91 (C), 169.57 (C), 170.36 (C) and 170.65 (C); LCMS [M+H]<sup>+</sup>=456.

1-c. Synthesis of 1,5-anhydro-2-deoxy-2-[(1,3-dimethyl-2,4,6- (1H, 3H, 5H)-trioxypyrimidin-5-ylidene) methylamino]-D-glucitol (4).

Compound **3** was treated as described by General Method 3 to provide **4**; *R<sub>f</sub>* (product)  $\approx$  0.00 in 1:1 ethyl acetate/light petroleum (40-60°C), (S.M  $\approx$  0.4). When system changed to 9:1 acetonitrile/methanol, *R<sub>f</sub>* (product)  $\approx$  0.4. (S.M  $\approx$  1.0); ,  $\delta_{\text{H}}$  (400 MHz; DMSO) 3.13 (3 H, s), 3.14 (3 H, s), 3.47 (3 H, m), 3.65 (3 H, dd), 3.85 (1 H, d, *J* 6.0 Hz), 4.52 (1 H, t, *J* 5.8 Hz), 5.11 (1 H, d, *J* 4.8 Hz), 5.28 (1 H, d, *J* 5.6 Hz), 8.18 (1 H, d, *J* 14.4 Hz) and 10.03 (1 H, br t, *J* 8.4 Hz);  $\delta_{\text{C}}$  (400 MHz; DMSO) 27.63 (CH<sub>3</sub>), 28.29 (CH<sub>3</sub>), 62.00 (CH<sub>2</sub>), 62.90 (CH), 67.68 (CH<sub>2</sub>), 71.37 (CH), 75.42 (CH), 82.22 (CH), 152.18 (C  $\times$  2), 160.18 (CH), 162.71 (C) and 164.37 (C); LCMS [M+H]<sup>+</sup>=330.

30 1-d. Synthesis of 1,5-anhydro-2-deoxy-2-[(1,3-dimethyl-2,4,6- (1H, 3H, 5H)-trioxypyrimidin-5-ylidene) methylamino]-4,6-O-(4-methoxybenzylidene)-D-glucitol (5).

Compound **4** was treated as described by General Method 4, to give the desired product **5** as a solid (86%); *R<sub>f</sub>* (product)  $\approx$  0.1 in 1:1 ethyl acetate/light

- petroleum (40-60°C),  $\delta_H$  (400 MHz;  $CDCl_3$ ) 3.29 (3 H, s), 3.30 (3 H, s), 3.48 (5 H, m), 3.70 (1 H, t,  $J$  10.2 Hz), 3.81 (3 H, s), 3.83 (1 H, m), 4.11 (1 H, m), 4.32 (1 H, dd,  $J$  10.4 Hz and  $J$  4.8 Hz), 5.51 (1 H, s), 6.90 (2 H, d,  $J$  8.8 Hz), 7.40 (2 H, d,  $J$  8.4 Hz), 8.24 (1 H, d,  $J$  13.6 Hz) and 10.20 (1 H, br t,  $J$  11.5 Hz);
- 5 LCMS  $[M+H]^+=448$ .

1-e. Synthesis of 1,5-anhydro-3-O-(4-chlorobenzoyl)-2-deoxy-2-[(1,3-dimethyl-2,4,6- (1H, 3H, 5H)-trioxypyrimidin-5-ylidene) methylamino]-4,6-O-(4-methoxybenzylidene)-D-glucitol (6).

- 10 Compound 5 was treated according to General Method 5, to give the product 6 as a off-white solid (83%);  $R_f$  (product)  $\approx$  0.33 in 1:1 ethyl acetate/light petroleum (40-60°C). (S.M  $\approx$  0.17);  $\delta_H$  (400 MHz;  $CDCl_3$ ) 3.24 (3 H, s), 3.25 (3 H, s), 3.72 (8 H, m), 4.14 (1 H, t,  $J$  5.5 Hz), 4.35 (1 H, t,  $J$  5.4 Hz), 5.50 (1 H, s), 5.57 (1 H, t,  $J$  9.6 Hz), 6.82 (2 H, dd,  $J$  6.6 Hz and  $J$  2.2 Hz), 7.30 (2 H, dd,
- 15  $J$  6.8 Hz and  $J$  2.0 Hz), 7.38 (2 H, dd,  $J$  6.8 Hz and  $J$  2.0 Hz), 7.93 (2 H, dd,  $J$  6.6 Hz and  $J$  2.2 Hz), 8.12 (1 H, d,  $J$  13.6 Hz), and 10.20 (1 H, br t,  $J$  11.6 Hz); LCMS  $[M+H]^+=586$ .

- 1-f. Synthesis of 1,5-anhydro-3-O-(4-chlorobenzoyl)-2-deoxy-2-[(1,3-dimethyl-2,4,6- (1H, 3H, 5H)-trioxypyrimidin-5-ylidene) methylamino]-6-O-(4-methoxybenzyl)-D-glucitol (7).
- 20

- Compound 6 was treated according to the procedure described in General Method 33 to give the product 7 as an off-white foam (93%);  $R_f$  (product)  $\approx$  0.26 in 1:1 ethyl acetate/light petroleum (40-60°C). (S.M  $\approx$  0.33);  $\delta_H$  (400
- 25 MHz;  $CDCl_3$ ) 3.23 (3 H, s), 3.24 (3 H, s), 3.51 (2 H, m), 3.80 (8 H, m), 4.13 (1 H, dd,  $J$  11.4 Hz and  $J$  5.4 Hz), 4.52 (2 H, q,  $J$  11.2 Hz), 5.27 (1 H, t,  $J$  9.6 Hz), 6.87 (2 H, d,  $J$  8.8 Hz), 7.26 (2 H, m), 7.40 (2 H, d,  $J$  8.8 Hz), 7.93 (2 H, d,  $J$  8.8 Hz), 8.11 (1 H, d,  $J$  13.6 Hz), and 10.30 (1 H, br t,  $J$  11.5 Hz); LCMS  $[M+H]^+=588$ .

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1-g. Synthesis of 1,5-anhydro-4-azido-3-O-(4-chlorobenzoyl)-2,4-dideoxy-2-[(1,3-dimethyl-2,4,6- (1H, 3H, 5H)-trioxypyrimidin-5-ylidene) methylamino]-6-O-(4-methoxybenzyl)-D-galactitol (8).



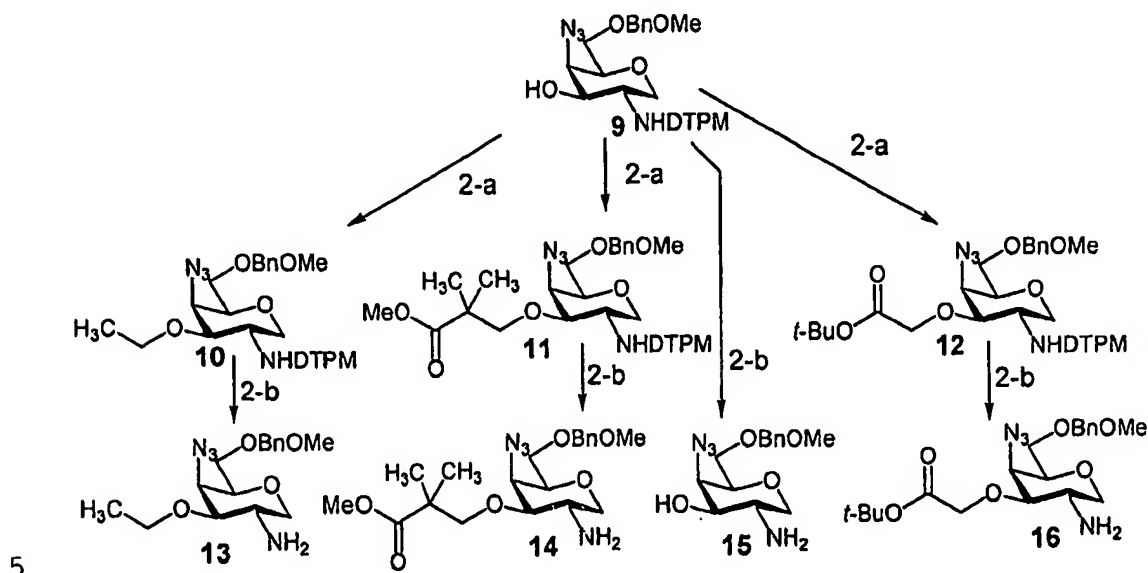
Compound 7 was treated according to the procedure described in General Method 6 to give compound 8, (93%)  $R_f$  (product)  $\approx$  0.62 in 1:1 ethyl acetate/light petroleum. Product recrystallised from isopropanol; LCMS  $[M+H]^+=613$ .

5

1-h. Synthesis of 1,5-anhydro-4-azido-3-O-(4-chlorobenzoyl)-2,4-dideoxy-2-[(1,3-dimethyl-2,4,6-(1H, 3H, 5H)-trioxypyrimidin-5-ylidene) methylamino]-D-galactitol (9).

10 Compound 8 was reacted according to General Method 3, to give the desired product 9 (70%) as a white foam,  $\delta_H$  (400 MHz;  $CDCl_3$ ) 3.25 (3 H, s), 3.26 (3 H, s), 3.65 (5 H, m), 3.80 (3 H, s), 4.09 (3 H, m), 4.50 (2 H, q,  $J$  9.5 Hz and  $J$  3.6 Hz), 6.89 (2 H, d,  $J$  8.8 Hz), 7.26 (2 H, d,  $J$  8.8 Hz), 8.21 (1 H, d,  $J$  13.6 Hz), and 10.15 (1 H, br t,  $J$  11.4 Hz); LCMS  $[M+H]^+=475$ .

Example 2: Synthesis of a Galactitol Library - Preparation of Intermediates:  
General Procedures for Alkylation of the C-3 Position and Removal of the  
DTPM Group



2-a. Alkylation of the C-3 Position: Preparation of compounds 10, 11 and 12.

Compounds 10, 11, and 12 were prepared according to General Method 7.

Analytical Data

| Compound No. | 10  | 11  | 12  |
|--------------|-----|-----|-----|
| $[M+H]^+$    | 503 | 589 | 589 |

10

2-b. Removal of the DTPM Group at the C-2 Position. Preparation of  
Compounds 13, 14, 15 and 16.

Compounds 13, 14, 15, and 16 were prepared according to General Method 8.

15 Analytical Data.

| Compound  | 13  | 14  | 15  | 16  |
|-----------|-----|-----|-----|-----|
| $[M+H]^+$ | 337 | 423 | 309 | 423 |

Data for 5-Azido-4-ethoxy-6-(4-methoxy-benzyloxymethyl)-tetrahydro-pyran-3-  
ylamine (13)

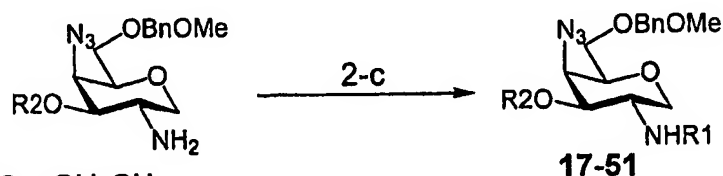
Yellow oil, yield (100 %),  $\delta_H$  (400 MHz;  $CDCl_3$ ) 1.27 (3 H, t,  $J$  7.0 Hz), 1.50 (2  
 20 H, br s), 3.06 (1 H, t,  $J$  11.0 Hz), 3.21 (2 H, m), 3.52 (4 H, m), 3.78 (4 H, m),  
 3.93 (1 H, dd,  $J$  10.8 Hz and  $J$  4.6 Hz), 4.04 (1 H, d,  $J$  3.2 Hz), 4.48 (2 H, q,  $J$

14.8 Hz and  $J$  11.6 Hz), 6.88 (2 H, d,  $J$  8.4 Hz) and 7.26 (2 H, d,  $J$  8.8 Hz); LCMS  $[M+H]^+ = 337$ .

## 2-c. Preparation of Intermediates: General Procedures from Preparation of

### 5 Derivatives at the C-2 Position

Compounds **17** to **51** were individually prepared according to one of General Methods 9, 10, 11 and 12.



13.  $R_2 = CH_2CH_3$

14.  $R_2 = CH_2C(CH_3)_2C(O)OMe$

15.  $R_2 = H$

16.  $R_2 = CH_2C(O)O^tBu$

10

*Analytical Data: Example of a product of General Method 9: [3-Azido-5-(3-tert-butoxycarbonylamino-propionylamino)-2-(4-methoxy-benzyloxymethyl)-tetrahydro-pyran-4-yloxy]-acetic acid tert-butyl ester (33)*

Sugar (**16**) (3.1 mmol) coupled to Boc- $\beta$ -alanine (3.2 mmol) gave the title compound (**33**) as an off-white solid, in 69% yield after column chromatography (silica; 50% ethyl acetate in light petroleum (40-60°C)),  $\delta_H$  (400 MHz;  $CDCl_3$ ) 1.42 (9 H, s), 1.49 (9 H, s), 2.43 (2 H, t,  $J$  6.4 Hz), 2.95 (1 H, t,  $J$  10.2 Hz), 3.48 (6 H, m), 3.81 (3 H, s), 4.07 (4 H, m), 4.47 (3 H, q,  $J$  11.4 Hz and  $J$  6.8 Hz), 5.24 (1 H, br. s.), 6.89 (2 H, d,  $J$  8.8 Hz), 7.25 (2 H, d,  $J$  8.4 Hz) and 7.51 (1 H, br. d,  $J$  5.2 Hz); LCMS  $[M+H]^+ = 594$ .

20

*Example of a Product of General Method 9: Acetic acid [5-azido-4-hydroxy-6-(4-methoxy-benzyloxymethyl)-tetrahydro-pyran-3-ylcarbamoyl]-methyl ester (45)*

Sugar (**15**) (4.2 mmol), was coupled to acetoxycetic acid (4.3 mmol) and after trituration with diethyl ether gave the title compound (**45**) as a white solid in 64%,  $\delta_H$  (400 MHz;  $CDCl_3$ ) 2.17 (3 H, s), 3.19 (1 H, t,  $J$  10.8 Hz), 3.44 (1 H,

25

d,  $J$  7.2 Hz), 3.60 (3 H, m), 3.76 (1 H, m), 3.80 (3 H, s), 4.06 (3 H, m), 4.49 (2 H, q,  $J$  10.2 Hz and  $J$  2.4 Hz), 4.56 (2 H, s), 6.04 (1 H, d,  $J$  6.8 Hz), 6.89 (2 H, d,  $J$  6.8 Hz) and 7.26 (2 H, d,  $J$  8.8 Hz); LCMS  $[M+H+Na]^+=431$ .

5 *Example of a product of General Method 9: N-[5-Azido-4-hydroxy-6-(4-methoxy-benzyloxymethyl)-tetrahydro-pyran-3-yl]-succinamic acid methyl ester (18)*

Sugar (15) (4.5 mmol), coupled to succinic acid mono methyl ester (4.8 mmol), after trituration with diethyl ether gave the title compound (18) (63%),  
10 as a white solid;  $\delta_H$  (400 MHz; DMSO) 2.35 (2 H, dt,  $J$  6.9 Hz and  $J$  2.4 Hz), 2.47 (2 H, t,  $J$  6.8 Hz), 2.89 (1 H, t,  $J$  10.8 Hz), 3.43 (2 H, dd,  $J$  5.8 Hz and 2.6 Hz), 3.56 (3 H, s), 3.64 (2 H, dd,  $J$  11.0 Hz and  $J$  5.0 Hz), 3.73 (3 H, s), 3.80 (3 H, m), 4.39 (2 H, q,  $J$  10.9 Hz), 5.48 (1 H, d,  $J$  4.4 Hz), 6.89 (2 H, dd,  $J$  6.4 Hz and  $J$  2.8 Hz), 7.23 (2 H, d,  $J$  8.8 Hz) and 7.73 (1 H, d,  $J$  8.0 Hz);  $\delta_C$  (400  
15 MHz; DMSO) 29.65 (CH<sub>3</sub>), 30.80 (CH<sub>3</sub>), 48.62 (CH<sub>2</sub>), 52.12 (CH<sub>2</sub>), 55.86 (CH<sub>2</sub>), 63.92 (CH<sub>2</sub>), 68.56 (CH), 69.85 (CH), 72.18 (CH), 72.76 (CH), 76.20 (CH<sub>2</sub>), 114.30 (CH  $\times$  2), 129.03 (CH  $\times$  2), 130.68 (C), 159.32 (C), 171.73 (C) and 173.35 (C); LCMS  $[M+H+Na]^+=423$ .

20 *Example of a product of General Method 10; {3-[5-Azido-4-hydroxy-6-(4-methoxy-benzyloxymethyl)-tetrahydro-pyran-3-yl]-ureido}-acetic acid ethyl ester (41)*

Compound 41, white solid, yield 66%;  $\delta_H$  (400 MHz; DMSO) 1.17 (3 H, t,  $J$  6.8 Hz), 2.88 (1 H, t,  $J$  10.6 Hz), 3.31 (2 H, s), 3.42 (2 H, m), 3.67 (9 H, m), 3.85  
25 (1 H, dd,  $J$  3.2 Hz and  $J$  1.2 Hz), 4.06 (2 H, q,  $J$  7.0 Hz), 4.39 (2 H, q,  $J$  10.7 Hz), 5.56 (1 H, d,  $J$  4.4 Hz), 6.09 (1 H, d,  $J$  6.8 Hz), 6.28 (1 H, t,  $J$  5.8 Hz), 6.89 (1 H, d,  $J$  6.8 Hz) and 7.22 (1 H, d,  $J$  6.8 Hz);  $\delta_C$  (400 MHz; DMSO) 15.03 (CH<sub>3</sub>), 42.28 (CH<sub>2</sub>  $\times$  2), 49.30 (CH<sub>3</sub>), 55.88 (CH), 61.00 (CH<sub>2</sub>), 64.13 (CH), 69.47 (CH<sub>2</sub>), 69.84 (CH<sub>2</sub>), 72.74 (CH), 76.06 (CH), 114.30 (CH  $\times$  2),  
30 129.03 (CH  $\times$  2), 130.68 (C), 158.56 (C), 159.32 (C) and 171.57 (C); LCMS  $[M+H]^+=438$ .

*Example of a product of General Method 11: [5-Acetylamino-3-azido-2-(4-*

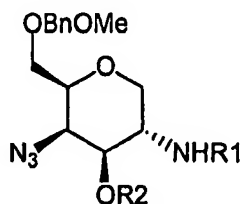
*methoxy-benzyloxy-methyl)-tetrahydro-pyran-4-yloxy]-acetic acid tert-butyl ester (36)*

Derivatisation of the *t*-butyl sugar (**16**) (3.1 mmol) gave the title compound **36** as a yellow oil, 89%,  $\delta_H$  (400 MHz;  $CDCl_3$ ) 1.43 (9 H, s,  $C(CH_3)_3$ ), 1.94 (3 H, s), 2.88 (1 H, t,  $J$  10.0 Hz), 3.45 (4 H, m), 3.74 (3 H, s), 4.04 (4 H, m), 4.40 (3 H, m), 6.82 (2 H, d,  $J$  8.8 Hz), 7.19 (2 H, d,  $J$  8.8 Hz) and 7.41 (1 H, br d,  $J$  5.2 Hz); LCMS  $[M+H]^+=465$ .

*Example of a product of General Method 12: 3-[3-Azido-2-(4-methoxy-benzyloxymethyl)-5-(2-methoxycarbonyl-acetylamino)-tetrahydro-pyran-4-yloxy]-2,2-dimethyl-propionic acid methyl ester (51)*

Derivatisation of the pivolate sugar (**14**) (3.6 mmol) gave the title compound as a brown oil (**51**) 75 %;  $\delta_H$  (400 MHz;  $CDCl_3$ ) 1.16 (3 H, s), 1.24 (3 H, s), 3.35 (3 H, m), 3.57 (6 H, m), 3.68 (3 H, s), 3.73 (3 H, s), 3.81 (3 H, s), 4.28 (3 H, m), 4.46 (2 H, q,  $J$  12.0 Hz and  $J$  11.6 Hz), 6.89 (2 H, d,  $J$  6.4 Hz) and 7.26 (2 H, d,  $J$  6.0 Hz); LCMS  $[M+H]^+=523$ .

The table below represents all compounds made with derivatives at the 2-position.

Table 1: Intermediates for synthesis of Galactitol Library.

5

| No. | R1* | R2* | Molecular Ion            | No. | R1  | R2  | Molecular Ion            |
|-----|-----|-----|--------------------------|-----|-----|-----|--------------------------|
| 17  | R1a | R2d | [M+H] <sup>+</sup> =537  | 35  | R1f | R2a | [M+H] <sup>+</sup> =508  |
| 18  | R1a | R2c | [M+Na] <sup>+</sup> =423 | 36  | R1g | R2d | [M+H] <sup>+</sup> =465  |
| 19  | R1a | R2a | [M+H] <sup>+</sup> =451  | 37  | R1g | R2c | [M+H] <sup>+</sup> =351  |
| 20  | R1a | R2b | [M+H] <sup>+</sup> =537  | 38  | R1g | R2a | [M+H] <sup>+</sup> =379  |
| 21  | R1b | R2d | [M+H] <sup>+</sup> =565  | 39  | R1g | R2b | [M+H] <sup>+</sup> =465  |
| 22  | R1b | R2c | [M+H] <sup>+</sup> =451  | 40  | R1h | R2d | [M+H] <sup>+</sup> =552  |
| 23  | R1b | R2a | [M+H] <sup>+</sup> =479  | 41  | R1h | R2c | [M+H] <sup>+</sup> =438  |
| 24  | R1c | R2d | [M+H] <sup>+</sup> =656  | 42  | R1h | R2a | [M+H] <sup>+</sup> =466  |
| 25  | R1c | R2c | [M+H] <sup>+</sup> =542  | 43  | R1h | R2b | [M+H] <sup>+</sup> =552  |
| 26  | R1c | R2a | [M+H] <sup>+</sup> =570  | 44  | R1i | R2d | [M+H] <sup>+</sup> =523  |
| 26  | R1d | R2d | [M+H] <sup>+</sup> =656  | 45  | R1i | R2c | [M+Na] <sup>+</sup> =431 |
| 28  | R1d | R2c | [M+H] <sup>+</sup> =542  | 46  | R1i | R2a | [M+H] <sup>+</sup> =437  |
| 29  | R1d | R2a | [M+H] <sup>+</sup> =570  | 47  | R1i | R2b | [M+H] <sup>+</sup> =523  |
| 30  | R1e | R2d | [M+H] <sup>+</sup> =613  | 48  | R1j | R2d | [M+H] <sup>+</sup> =523  |
| 31  | R1e | R2c | [M+H] <sup>+</sup> =499  | 49  | R1j | R2c | [M+H] <sup>+</sup> =409  |
| 32  | R1e | R2a | [M+H] <sup>+</sup> =527  | 50  | R1j | R2a | [M+H] <sup>+</sup> =437  |
| 33  | R1f | R2d | [M+H] <sup>+</sup> =594  | 51  | R1j | R2b | [M+H] <sup>+</sup> =523  |
| 34  | R1f | R2c | [M+H] <sup>+</sup> =480  |     |     |     |                          |

\*Sidearms for Tables 1 and 2 can be found at the end of Table 2.

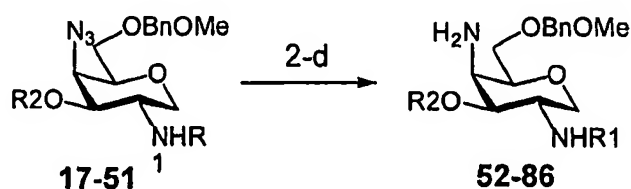
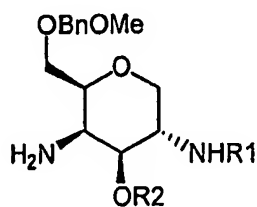
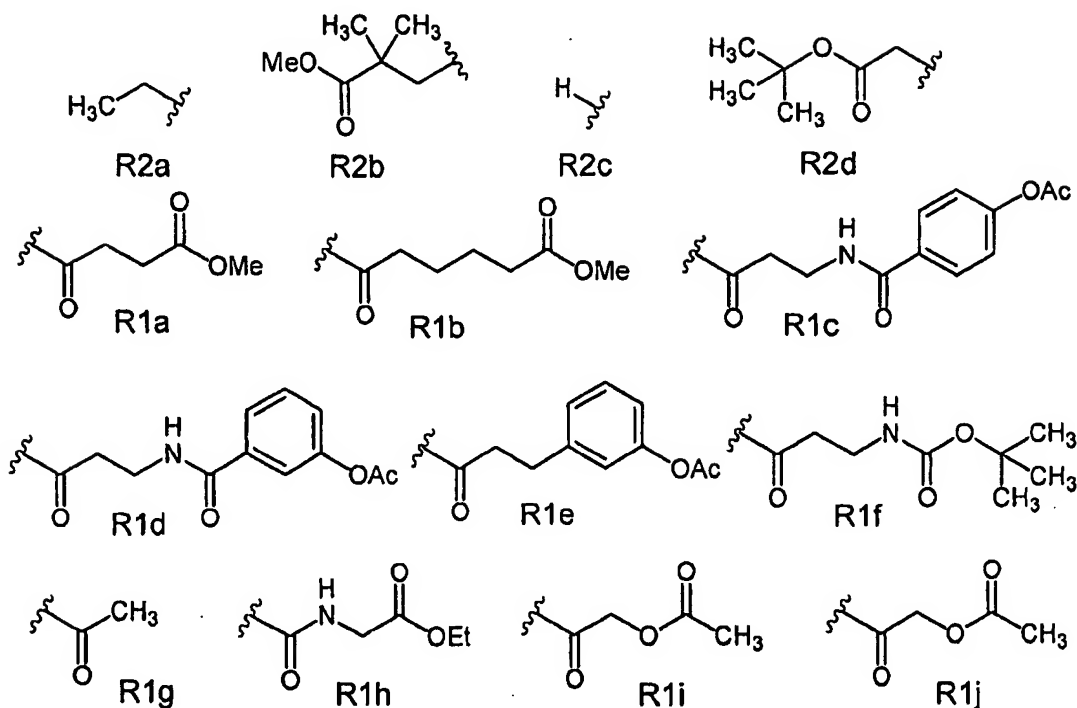
2-d. Preparation of derivatives reduced at the C-4 Position10 Compounds **52** to **86** were prepared according to General Method 13.

Table 2: Observed molecular ions of reduced azides

5

| No. | R1  | R2  | Molecular ion                        | No. | R1  | R2  | Molecular ion   |
|-----|-----|-----|--------------------------------------|-----|-----|-----|-----------------|
| 52  | R1a | R2d | $[M+H]^+ = 511$                      | 70  | R1f | R2a | $[M+H]^+ = 482$ |
| 53  | R1a | R2c | $[M+H]^+ = 397$                      | 71  | R1g | R2d | $[M+H]^+ = 439$ |
| 54  | R1a | R2a | $[M+H]^+ = 425$                      | 72  | R1g | R2c | No Data         |
| 55  | R1a | R2b | No Data                              | 73  | R1g | R2a | $[M+H]^+ = 353$ |
| 56  | R1b | R2d | $[M+H]^+ = 539$                      | 74  | R1g | R2b | $[M+H]^+ = 439$ |
| 57  | R1b | R2c | $[M+H]^+ = 425$                      | 75  | R1h | R2d | $[M+H]^+ = 526$ |
| 58  | R1b | R2a | $[M+H]^+ = 453$                      | 76  | R1h | R2c | $[M+H]^+ = 412$ |
| 59  | R1c | R2d | $[M+H]^+ = 588$                      | 77  | R1h | R2a | $[M+H]^+ = 440$ |
| 60  | R1c | R2c | $[M+H]^+ = 474$<br>(loss of acetate) | 78  | R1h | R2b | $[M+H]^+ = 526$ |
| 61  | R1c | R2a | $[M+H]^+ = 502$<br>(loss of acetate) | 79  | R1i | R2d | $[M+H]^+ = 497$ |
| 62  | R1d | R2d | $[M+H]^+ = 588$                      | 80  | R1i | R2c | $[M+H]^+ = 383$ |
| 63  | R1d | R2c | $[M+H]^+ = 474$<br>(loss of acetate) | 81  | R1i | R2a | $[M+H]^+ = 411$ |
| 64  | R1d | R2a | $[M+H]^+ = 544$                      | 82  | R1i | R2b | $[M+H]^+ = 497$ |
| 65  | R1e | R2d | $[M+H]^+ = 587$                      | 83  | R1j | R2d | $[M+H]^+ = 497$ |
| 66  | R1e | R2c | $[M+H]^+ = 431$<br>(loss of acetate) | 84  | R1j | R2c | $[M+H]^+ = 383$ |
| 67  | R1e | R2a | $[M+H]^+ = 501$                      | 85  | R1j | R2a | $[M+H]^+ = 411$ |
| 68  | R1f | R2d | $[M+H]^+ = 568$                      | 86  | R1j | R2b | $[M+H]^+ = 497$ |
| 69  | R1f | R2c | $[M+H]^+ = 454$                      |     |     |     |                 |

**Sidearms for Example 2: Tables 1 and 2.**



5

### 2-e. Final *N*-Acylation of Galactitol Derivatives in the C-4 position.

Compounds **87** to **416** were prepared in an automated fashion using chemistries according to General Method 9. As required, protecting groups on the sidearms, or the ring were hydrolytically cleaved in either a base or acid catalysed fashion, using either General Method 14 or 15.

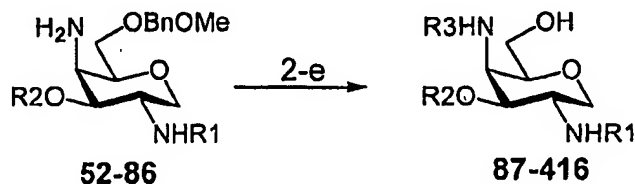
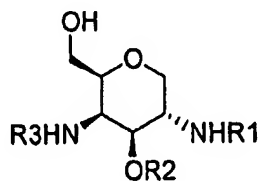




Table 3: Library of 1,5-Anhydro-galactitol Compounds

5

| Compound No. | R1  | R2  | R3  | Yield | Retention Time (mins) | HPLC Method |
|--------------|-----|-----|-----|-------|-----------------------|-------------|
| 87           | R1a | R2a | R3a | 70    | 4.72                  | A           |
| 88           | R1a | R2a | R3b | 83    | 4.28                  | A           |
| 89           | R1a | R2a | R3c | 74    | 4.90                  | A           |
| 90           | R1a | R2a | R3d | 38    | 4.44                  | A           |
| 91           | R1a | R2a | R3e | 10    | 4.73                  | A           |
| 92           | R1a | R2a | R3f | 44    | 4.53                  | A           |
| 92           | R1b | R2a | R3b | 64    | 4.73                  | A           |
| 94           | R1b | R2a | R3g | 77    | 4.35                  | A           |
| 95           | R1c | R2a | R3h | 82    | 5.33                  | A           |
| 96           | R1c | R2a | R3a | 50    | 4.28                  | A           |
| 97           | R1c | R2a | R3c | 42    | 4.00                  | A           |
| 98           | R1c | R2a | R3d | 85    | 4.46                  | A           |
| 99           | R1c | R2a | R3f | 21    | 4.62                  | A           |
| 100          | R1d | R2a | R3h | 84    | 4.55                  | A           |
| 101          | R1d | R2a | R3a | 100   | 4.56                  | A           |
| 102          | R1d | R2a | R3b | 91    | 4.72                  | A           |
| 103          | R1d | R2a | R3c | 70    | 4.64                  | A           |
| 104          | R1d | R2a | R3d | 92    | 5.27                  | A           |
| 105          | R1d | R2a | R3f | 50    | 4.73                  | A           |
| 106          | R1e | R2a | R3i | 100   | 3.54                  | A           |
| 107          | R1e | R2a | R3i | 61    | 4.53                  | A           |
| 108          | R1e | R2a | R3b | 97    | 5.74                  | A           |
| 109          | R1e | R2a | R3d | 93    | 6.02                  | A           |
| 110          | R1e | R2a | R3e | 10    | 6.18                  | A           |
| 111          | R1e | R2a | R3f | 62    | 5.74                  | A           |
| 112          | R1f | R2a | R3b | 80    | 4.55                  | A           |
| 113          | R1f | R2a | R3d | 36    | 5.17                  | A           |
| 114          | R1g | R2a | R3j | 100   | 4.55                  | A           |
| 115          | R1g | R2a | R3k | 96    | 5.36                  | A           |
| 116          | R1g | R2a | R3l | 100   | 6.66                  | A           |
| 117          | R1g | R2a | R3m | 100   | 7.01                  | A           |
| 118          | R1g | R2a | R3n | 100   | 6.39                  | A           |
| 119          | R1g | R2a | R3o | 97    | 4.44                  | A           |
| 120          | R1g | R2a | R3o | 95    | 4.37                  | A           |
| 121          | R1g | R2a | R3p | 90    | 5.40                  | A           |
| 122          | R1f | R2a | R3j | 90    | 4.92                  | A           |
| 123          | R1f | R2a | R3k | 93    | 5.14                  | A           |
| 124          | R1f | R2a | R3n | 96    | 6.84                  | A           |
| 125          | R1f | R2a | R3n | 95    | 7.19                  | A           |
| 126          | R1f | R2a | R3o | 72    | 6.48                  | A           |

|     |     |     |     |      |      |   |
|-----|-----|-----|-----|------|------|---|
| 127 | R1f | R2a | R3q | 63   | 2.60 | A |
| 128 | R1h | R2a | R3l | 79   | 4.07 | A |
| 129 | R1h | R2a | R3m | 77   | 3.52 | A |
| 130 | R1h | R2a | R3n | 100  | 4.09 | A |
| 131 | R1h | R2a | R3o | 54   | 5.36 | A |
| 132 | R1h | R2a | R3q | 74   | 5.50 | A |
| 133 | R1h | R2a | R3p | 91   | 3.78 | A |
| 134 | R1i | R2a | R3m | 79   | 4.05 | A |
| 135 | R1i | R2a | R3r | 77.5 | 1.50 | A |
| 136 | R1i | R2a | R3s | 69   | 3.77 | A |
| 137 | R1i | R2a | R3t | 100  | 5.26 | A |
| 138 | R1i | R2a | R3n | 93   | 5.38 | A |
| 139 | R1i | R2a | R3v | 71   | 3.83 | A |
| 140 | R1j | R2a | R3m | 87   | 4.79 | A |
| 141 | R1j | R2a | R3n | 95   | 5.65 | A |
| 142 | R1j | R2a | R3r | 78   | 5.08 | A |
| 143 | R1j | R2a | R3s | 81   | 5.65 | A |
| 144 | R1j | R2a | R3t | 98   | 5.27 | A |
| 145 | R1j | R2a | R3n | 93   | 5.08 | A |
| 146 | R1j | R2a | R3v | 99   | 4.92 | A |
| 147 | R1b | R2a | R3m | 90   | 4.92 | A |
| 148 | R1b | R2a | R3n | 45   | 5.10 | A |
| 149 | R1b | R2a | R3r | 97   | 5.17 | A |
| 150 | R1b | R2a | R3s | 89   | 5.19 | A |
| 151 | R1b | R2a | R3t | 82   | 5.54 | A |
| 152 | R1b | R2a | R3n | 95   | 5.63 | A |
| 153 | R1b | R2a | R3v | 62   | 6.39 | A |
| 154 | R1a | R2b | R3b | 95   | 6.73 | A |
| 155 | R1a | R2b | R3d | 100  | 7.49 | A |
| 156 | R1b | R2b | R3b | 97   | 6.37 | A |
| 157 | R1b | R2b | R3d | 97   | 5.00 | A |
| 158 | R1c | R2b | R3w | 16.5 | 7.47 | A |
| 159 | R1c | R2b | R3b | 98.5 | 5.27 | A |
| 160 | R1c | R2b | R3d | 99   | 5.01 | A |
| 161 | R1c | R2b | R3g | 40   | 4.09 | A |
| 162 | R1d | R2b | R3b | 70.5 | 4.72 | A |
| 163 | R1d | R2b | R3d | 69   | 5.74 | A |
| 164 | R1d | R2b | R3g | 95   | 5.19 | A |
| 165 | R1e | R2b | R3w | 80   | 4.62 | A |
| 166 | R1e | R2b | R3b | 100  | 4.28 | A |
| 167 | R1e | R2b | R3d | 100  | 4.62 | A |
| 168 | R1e | R2b | R3g | 63   | 4.28 | A |
| 169 | R1f | R2b | R3d | 97   | 4.44 | A |
| 170 | R1f | R2b | R3j | 100  | 4.37 | A |
| 171 | R1f | R2b | R3k | 91   | 4.62 | A |
| 172 | R1f | R2b | R3l | 97   | 4.18 | A |
| 173 | R1f | R2b | R3m | 65   | 4.07 | A |
| 174 | R1f | R2b | R3x | 91   | 4.64 | A |
| 175 | R1f | R2b | R3q | 54   | 4.99 | A |
| 176 | R1h | R2b | R3j | 85   | 6.94 | A |
| 177 | R1h | R2b | R3k | 100  | 6.09 | A |
| 178 | R1h | R2b | R3l | 100  | 4.92 | A |
| 179 | R1h | R2b | R3m | 92   | 4.53 | A |
| 180 | R1h | R2b | R3x | 90   | 5.19 | A |
| 181 | R1i | R2b | R3m | 83   | 4.61 | A |

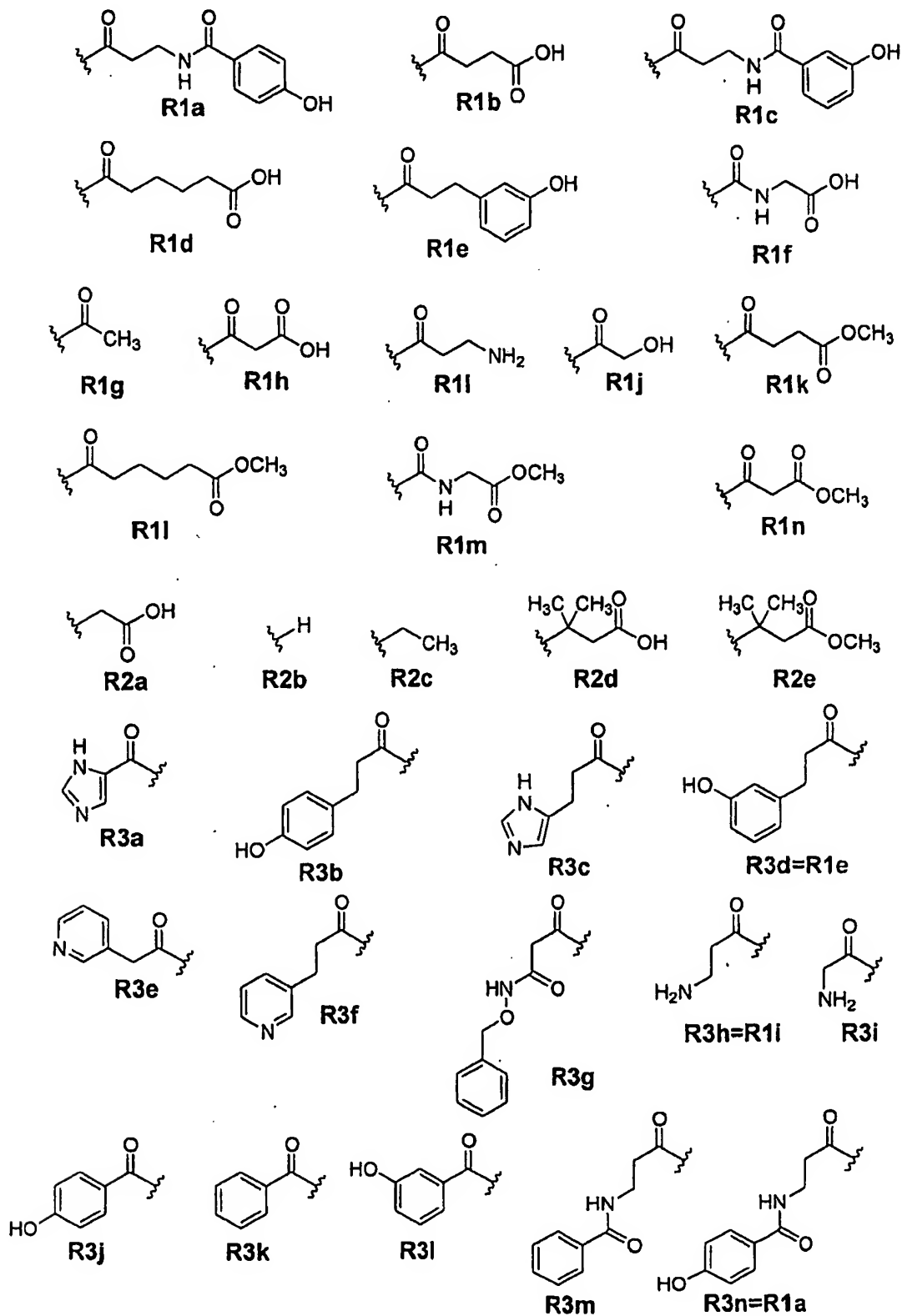
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|-----|-----|-----|-----|-----|------|---|
| 182 | R1i | R2b | R3p | 15  | 1.69 | A |
| 183 | R1i | R2b | R3r | 100 | 4.09 | A |
| 184 | R1i | R2b | R3s | 100 | 1.69 | A |
| 185 | R1i | R2b | R3t | 96  | 4.18 | A |
| 186 | R1i | R2b | R3u | 100 | 4.46 | A |
| 187 | R1i | R2b | R3v | 100 | 4.94 | A |
| 188 | R1j | R2b | R3m | 97  | 1.71 | A |
| 189 | R1j | R2b | R3p | 98  | 1.69 | A |
| 190 | R1j | R2b | R3r | 84  | 2.07 | A |
| 191 | R1j | R2b | R3s | 100 | 2.26 | A |
| 192 | R1j | R2b | R3t | 100 | 1.69 | A |
| 193 | R1j | R2b | R3u | 70  | 2.26 | A |
| 194 | R1j | R2b | R3v | 100 | 1.6  | A |
| 195 | R1j | R2b | R3g | 100 | 3.00 | A |
| 196 | R1a | R2c | R3w | 100 | 4.41 | A |
| 197 | R1a | R2c | R3a | 50  | 0.55 | A |
| 198 | R1a | R2c | R3b | 96  | 1.78 | A |
| 199 | R1a | R2c | R3c | 58  | 1.69 | A |
| 200 | R1a | R2c | R3d | 95  | 2.35 | A |
| 201 | R1a | R2c | R3f | 32  | 2.26 | A |
| 202 | R1a | R2c | R3g | 6   | 4.14 | A |
| 203 | R1b | R2c | R3b | 100 | 3.94 | A |
| 204 | R1b | R2c | R3d | 100 | 4.75 | A |
| 205 | R1b | R2c | R3f | 32  | 4.9  | A |
| 206 | R1b | R2c | R3i | 83  | 1.8  | A |
| 207 | R1c | R2c | R3w | 77  | 1.69 | A |
| 208 | R1c | R2c | R3a | 44  | 2.17 | A |
| 209 | R1c | R2c | R3b | 99  | 4.33 | A |
| 210 | R1c | R2c | R3c | 43  | 2.26 | A |
| 211 | R1c | R2c | R3d | 93  | 3.34 | A |
| 212 | R1d | R2c | R3c | 94  | 4.18 | A |
| 213 | R1d | R2c | R3d | 90  | 5.36 | A |
| 214 | R1d | R2c | R3e | 15  | 2.17 | A |
| 215 | R1d | R2c | R3f | 91  | 1.89 | A |
| 216 | R1e | R2c | R3i | 100 | 1.78 | A |
| 217 | R1e | R2c | R3w | 97  | 4.55 | A |
| 218 | R1e | R2c | R3a | 80  | 6.20 | A |
| 219 | R1e | R2c | R3b | 94  | 3.25 | A |
| 220 | R1e | R2c | R3c | 62  | 4.09 | A |
| 221 | R1e | R2c | R3d | 91  | 4.35 | A |
| 222 | R1e | R2c | R3f | 37  | 4.48 | A |
| 223 | R1f | R2c | R3b | 100 | 4.83 | A |
| 224 | R1f | R2c | R3d | 96  | 5.28 | A |
| 225 | R1g | R2c | R3j | 100 | 1.78 | A |
| 226 | R1g | R2c | R3k | 100 | 4.00 | A |
| 227 | R1g | R2c | R3l | 100 | 4.00 | A |
| 228 | R1g | R2c | R3m | 100 | 5.74 | A |
| 229 | R1g | R2c | R3x | 100 | 3.73 | A |
| 230 | R1g | R2c | R3o | 100 | 5.10 | A |
| 231 | R1g | R2c | R3q | 100 | 4.09 | A |
| 232 | R1g | R2c | R3p | 98  | 5.56 | A |
| 233 | R1g | R2c | R3r | 95  | 6.55 | A |
| 234 | R1f | R2c | R3j | 88  | 6.39 | A |
| 235 | R1f | R2c | R3k | 85  | 5.13 | A |
| 236 | R1f | R2c | R3l | 89  | 4.78 | A |

|     |     |     |     |     |      |   |
|-----|-----|-----|-----|-----|------|---|
| 237 | R1f | R2c | R3m | 94  | 3.82 | A |
| 238 | R1f | R2c | R3x | 84  | 4.09 | A |
| 239 | R1f | R2c | R3o | 98  | 3.08 | A |
| 240 | R1f | R2c | R3q | 98  | 3.54 | A |
| 241 | R1f | R2c | R3p | 94  | 3.73 | A |
| 242 | R1h | R2c | R3j | 100 | 3.91 | A |
| 243 | R1h | R2c | R3k | 86  | 5.36 | A |
| 244 | R1h | R2c | R3l | 98  | 4.83 | A |
| 245 | R1h | R2c | R3m | 96  | 2.35 | A |
| 246 | R1h | R2c | R3x | 100 | 5.28 | A |
| 247 | R1f | R2c | R3r | 88  | 5.13 | A |
| 248 | R1h | R2c | R3o | 97  | 4.78 | A |
| 249 | R1h | R2c | R3q | 98  | 4.88 | A |
| 250 | R1h | R2c | R3p | 98  | 4.53 | A |
| 251 | R1h | R2c | R3q | 100 | 4.68 | A |
| 252 | R1l | R2c | R3m | 91  | 4.73 | A |
| 253 | R1i | R2c | R3p | 100 | 4.88 | A |
| 254 | R1i | R2c | R3s | 98  | 4.73 | A |
| 255 | R1i | R2c | R3t | 82  | 5.37 | A |
| 256 | R1i | R2c | R3u | 100 | 6.50 | A |
| 257 | R1i | R2c | R3v | 52  | 5.18 | A |
| 258 | R1j | R2c | R3m | 92  | 5.23 | A |
| 259 | R1j | R2c | R3p | 98  | 5.03 | A |
| 260 | R1j | R2c | R3r | 4   | 5.18 | A |
| 261 | R1j | R2c | R3s | 100 | 5.28 | A |
| 262 | R1j | R2c | R3t | 94  | 5.13 | A |
| 263 | R1j | R2c | R3u | 100 | 5.00 | A |
| 264 | R1j | R2c | R3v | 100 | 6.39 | A |
| 265 | R1j | R2c | R3g | 71  | 4.99 | A |
| 266 | R1b | R2c | R3m | 100 | 4.83 | A |
| 267 | R1b | R2c | R3p | 98  | 6.50 | A |
| 268 | R1b | R2c | R3r | 100 | 4.92 | A |
| 269 | R1b | R2c | R3s | 63  | 5.14 | A |
| 270 | R1b | R2c | R3t | 95  | 6.84 | A |
| 271 | R1b | R2c | R3u | 91  | 7.19 | A |
| 272 | R1b | R2c | R3v | 95  | 6.48 | A |
| 273 | R1b | R2d | R3i | 55  | 2.60 | A |
| 274 | R1b | R2d | R3w | 11  | 3.52 | A |
| 275 | R1b | R2d | R3a | 48  | 3.75 | A |
| 276 | R1b | R2d | R3b | 48  | 5.36 | A |
| 277 | R1b | R2d | R3d | 85  | 5.50 | A |
| 278 | R1b | R2d | R3e | 11  | 3.78 | A |
| 279 | R1b | R2d | R3f | 46  | 4.05 | A |
| 280 | R1f | R2d | R3i | 73  | 1.50 | A |
| 281 | R1f | R2d | R3w | 21  | 3.77 | A |
| 282 | R1f | R2d | R3b | 81  | 5.26 | A |
| 283 | R1f | R2d | R3d | 91  | 5.38 | A |
| 284 | R1f | R2d | R3f | 78  | 3.83 | A |
| 285 | R1g | R2d | R3j | 100 | 4.79 | A |
| 286 | R1g | R2d | R3k | 100 | 5.65 | A |
| 287 | R1g | R2d | R3l | 100 | 5.08 | A |
| 288 | R1g | R2d | R3m | 100 | 5.65 | A |
| 289 | R1g | R2d | R3o | 100 | 5.27 | A |
| 290 | R1g | R2d | R3r | 100 | 5.08 | A |
| 291 | R1f | R2d | R3j | 72  | 4.92 | A |

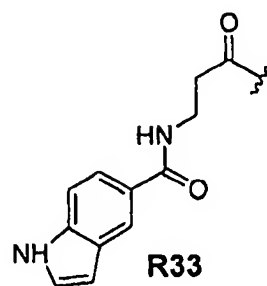
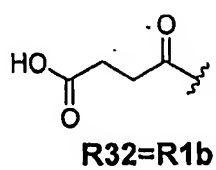
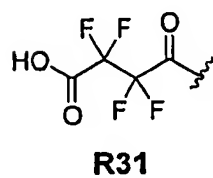
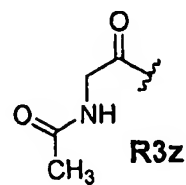
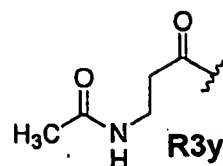
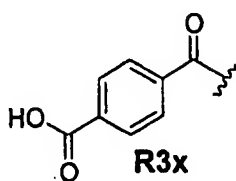
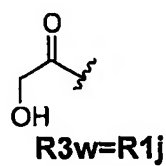
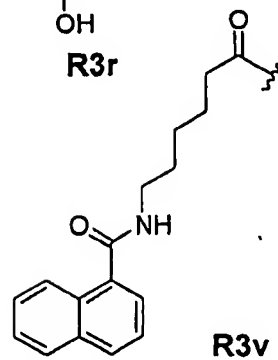
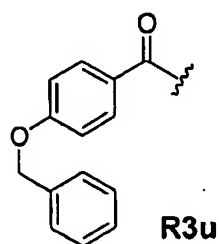
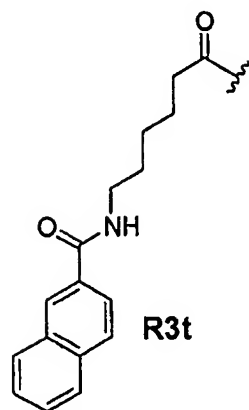
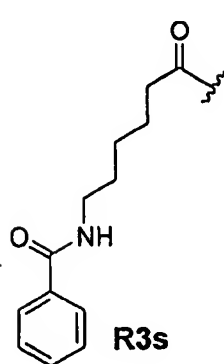
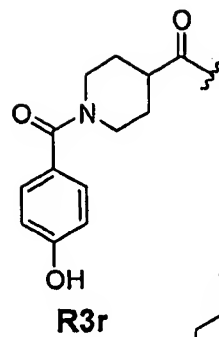
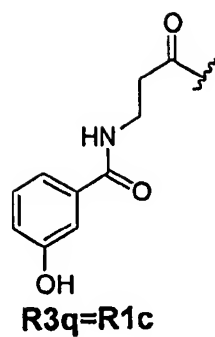
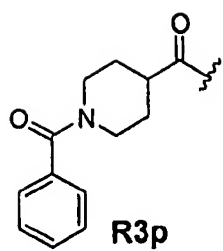
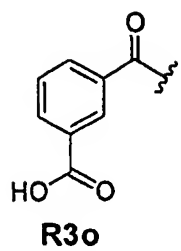
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|-----|-----|-----|-----|-----|------|---|
| 292 | R1f | R2d | R3l | 100 | 5.08 | A |
| 293 | R1f | R2d | R3x | 28  | 5.10 | A |
| 294 | R1f | R2d | R3o | 25  | 5.17 | A |
| 295 | R1f | R2d | R3r | 100 | 5.19 | A |
| 296 | R1h | R2d | R3k | 72  | 5.54 | A |
| 297 | R1j | R2d | R3p | 56  | 5.63 | A |
| 298 | R1j | R2d | R3r | 66  | 5.10 | A |
| 299 | R1j | R2d | R3t | 42  | 6.73 | A |
| 300 | R1j | R2d | R3u | 100 | 7.49 | A |
| 301 | R1j | R2d | R3v | 100 | 6.37 | A |
| 302 | R1b | R2d | R3r | 5   | 5.00 | A |
| 303 | R1b | R2d | R3u | 100 | 7.47 | A |
| 304 | R1c | R2a | R3b | 100 | 5.27 | A |
| 305 | R1e | R2a | R3w | 88  | 4.72 | A |
| 306 | R1a | R2a | R3y | 64  | 4.61 | A |
| 307 | R1b | R2a | R3h | 95  | 1.69 | A |
| 308 | R1b | R2a | R3w | 13  | 4.09 | A |
| 309 | R1b | R2a | R3a | 76  | 1.69 | A |
| 310 | R1b | R2a | R3f | 59  | 4.18 | A |
| 311 | R1c | R2a | R3y | 90  | 4.46 | A |
| 312 | R1e | R2a | R3z | 84  | 4.94 | A |
| 313 | R1f | R2a | R3i | 100 | 1.71 | A |
| 314 | R1f | R2a | R3w | 72  | 1.69 | A |
| 315 | R1f | R2a | R3a | 64  | 2.07 | A |
| 316 | R1f | R2a | R3e | 82  | 2.26 | A |
| 317 | R1f | R2a | R3f | 98  | 1.69 | A |
| 318 | R1i | R2a | R31 | 42  | 2.26 | B |
| 319 | R1i | R2a | R32 | 78  | 1.60 | B |
| 320 | R1j | R2a | R32 | 56  | 3.00 | B |
| 321 | R1a | R2b | R33 | 70  | 4.41 | A |
| 322 | R1a | R2b | R3f | 90  | 0.55 | A |
| 323 | R1b | R2b | R3w | 94  | 1.78 | B |
| 324 | R1b | R2b | R3c | 69  | 1.69 | B |
| 325 | R1b | R2b | R3e | 12  | 2.35 | B |
| 326 | R1d | R2b | R3i | 98  | 2.26 | B |
| 327 | R1d | R2b | R3z | 78  | 4.14 | A |
| 328 | R1d | R2b | R3w | 82  | 2.33 | B |
| 329 | R1e | R2b | R3z | 66  | 4.75 | A |
| 330 | R1e | R2b | R3c | 81  | 4.9  | B |
| 331 | R1f | R2b | R3l | 100 | 1.8  | B |
| 332 | R1f | R2b | R3w | 91  | 1.69 | B |
| 333 | R1f | R2b | R3c | 93  | 2.17 | B |
| 334 | R1a | R2c | R3z | 52  | 4.33 | A |
| 335 | R1b | R2c | R3i | 98  | 2.26 | B |
| 336 | R1b | R2c | R3a | 28  | 3.34 | B |
| 337 | R1d | R2c | R3z | 60  | 4.18 | A |
| 338 | R1e | R2c | R3z | 23  | 4.73 | A |
| 339 | R1f | R2c | R3l | 100 | 2.17 | B |
| 340 | R1f | R2c | R3z | 87  | 1.89 | A |
| 341 | R1f | R2c | R3c | 100 | 2.35 | B |
| 342 | R1f | R2c | R3f | 48  | 4.55 | B |
| 343 | R1b | R2d | R3s | 50  | 6.20 | A |
| 344 | R1a | R2b | R3i | 22  | 3.25 | A |
| 345 | R1a | R2b | R3w | 100 | 4.09 | A |
| 346 | R1a | R2c | R3e | 34  | 4.35 | A |

|     |     |     |     |     |      |   |
|-----|-----|-----|-----|-----|------|---|
| 347 | R1b | R2a | R3e | 53  | 4.48 | A |
| 348 | R1f | R2a | R3c | 76  | 1.78 | A |
| 349 | R1b | R2b | R3i | 85  | 1.48 | B |
| 350 | R1b | R2b | R3a | 19  | 1.78 | B |
| 351 | R1c | R2a | R3g | 41  | 5.74 | A |
| 352 | R1d | R2a | R3w | 80  | 3.73 | A |
| 353 | R1h | R2d | R3x | 46  | 5.13 | A |
| 354 | R1b | R2a | R3d | 62  | 5.00 | A |
| 355 | R1i | R2b | R32 | 53  | 1.41 | B |
| 356 | R1j | R2b | R32 | 75  | 1.67 | B |
| 357 | R1b | R2b | R32 | 41  | 1.72 | B |
| 358 | R1b | R2b | R3m | 52  | 4.88 | A |
| 359 | R1b | R2b | R3r | 84  | 4.49 | A |
| 360 | R1b | R2b | R3s | 64  | 5.57 | A |
| 361 | R1b | R2b | R3t | 63  | 6.87 | A |
| 362 | R1b | R2b | R3u | 100 | 7.13 | A |
| 363 | R1b | R2b | R3v | 51  | 6.44 | A |
| 364 | R1i | R2c | R32 | 100 | 59   | B |
| 365 | R1j | R2c | R32 | 42  | 3.36 | B |
| 366 | R1b | R2c | R32 | 60  | 4.1  | A |
| 367 | R1j | R2d | R32 | 7   | 4.14 | A |
| 368 | R1b | R2d | R32 | 25  | 4.53 | A |
| 369 | R1a | R2e | R3c | 87  | 4.26 | A |
| 370 | R1c | R2e | R3a | 85  | 4.46 | A |
| 371 | R1h | R2e | R3o | 53  | 4.73 | A |
| 372 | R1i | R2e | R3v | 100 | 5.57 | A |
| 373 | R1k | R2b | R3b | 25  | 5.19 | A |
| 374 | R1l | R2b | R3b | 95  | 5.28 | A |
| 375 | R1l | R2b | R3d | 100 | 5.38 | A |
| 376 | R1m | R2b | R3d | 50  | 4.73 | A |
| 377 | R1n | R2b | R3k | 53  | 4.55 | A |
| 378 | R1k | R2c | R3b | 72  | 5.36 | A |
| 379 | R1k | R2c | R3d | 54  | 5.56 | A |
| 380 | R1k | R2c | R3u | 74  | 7.68 | A |
| 381 | R1b | R2f | R3i | 47  | 4.48 | A |
| 382 | R1b | R2f | R3b | 90  | 5.68 | A |
| 383 | R1b | R2f | R3d | 84  | 5.78 | A |
| 384 | R1f | R2f | R3i | 69  | 4.28 | A |
| 385 | R1f | R2f | R3b | 83  | 5.58 | A |
| 386 | R1f | R2f | R3d | 89  | 5.68 | A |
| 387 | R1g | R2f | R3m | 45  | 5.68 | A |
| 388 | R1f | R2f | R3o | 66  | 5.48 | A |
| 389 | R1f | R2f | R3p | 32  | 5.27 | A |
| 390 | R1h | R2f | R3k | 59  | 6.28 | A |
| 391 | R1h | R2f | R3l | 91  | 5.65 | A |
| 392 | R1h | R2f | R3p | 97  | 5.82 | A |
| 393 | R1h | R2f | R3r | 97  | 5.01 | A |
| 394 | R1j | R2f | R3m | 81  | 5.28 | A |
| 395 | R1j | R2f | R3p | 91  | 5.78 | A |
| 396 | R1j | R2f | R3t | 92  | 6.78 | A |
| 397 | R1j | R2f | R3u | 99  | 7.33 | A |
| 398 | R1j | R2f | R3v | 100 | 6.63 | A |
| 399 | R1b | R2f | R3p | 89  | 5.91 | A |
| 400 | R1b | R2f | R3s | 82  | 6.18 | A |
| 401 | R1b | R2f | R3t | 100 | 7.03 | A |

|     |     |     |     |      |       |   |
|-----|-----|-----|-----|------|-------|---|
| 402 | R1b | R2f | R3u | 88   | 7.83  | A |
| 403 | R1l | R2b | R3i | 54   | 4.4   | A |
| 404 | R1c | R2e | R3i | 70   | 3.82  | A |
| 405 | R1l | R2a | R3c | 39   | 4.46  | B |
| 406 | R1l | R2c | R3z | 69   | 4.18  | A |
| 407 | R1f | R2f | R33 | 21   | 10.48 | A |
| 408 | R1h | R2f | R3m | 58   | 5.58  | A |
| 409 | R1h | R2f | R3x | 92   | 5.60  | A |
| 410 | R1j | R2f | R3g | 73   | 6.2   | A |
| 411 | R1b | R2f | R3m | 46   | 5.68  | A |
| 412 | R1k | R2b | R3r | 50   | 5.14  | A |
| 413 | R1k | R2b | R3s | 54   | 6.05  | A |
| 414 | R1k | R2b | R3t | 88.5 | 7.15  | A |
| 415 | R1k | R2b | R3u | 100  | 7.35  | A |
| 416 | R1k | R2b | R3v | 100  | 6.79  | A |

Functional Groups for Table 3 Galactitol Library





HPLC Methods for Compounds in Table 3.Method A

5

| Time | H <sub>2</sub> O% | MeCN% | Flow rate ml/min |
|------|-------------------|-------|------------------|
| 0    | 100               | 0     | 2                |
| 2    | 100               | 0     | 2                |
| 10   | 40                | 60    | 2                |
| 12   | 0                 | 100   | 2                |

Agilent SB Zorbax C18 4.6 x 50mm (5µm, 80Å)

LC Mobile Phase: Acetonitrile : Water 0.1% formic acid

10

Method B

| Time | H <sub>2</sub> O% | MeCN% | Flow rate ml/min |
|------|-------------------|-------|------------------|
| 0    | 100               | 0     | 2                |
| 1    | 100               | 0     | 2                |
| 7    | 65                | 35    | 2                |
| 8    | 0                 | 100   | 2                |
| 9    | 0                 | 100   | 2                |

Agilent SB Zorbax Phenyl 4.6 x 150mm (5µm)

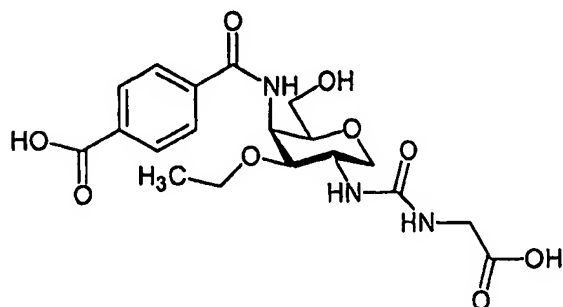
15

LC Mobile Phase: Acetonitrile : Water 0.1% formic acid

*<sup>1</sup>H-NMR Data for Three Compounds of Final Library.*

**Compound (238)**

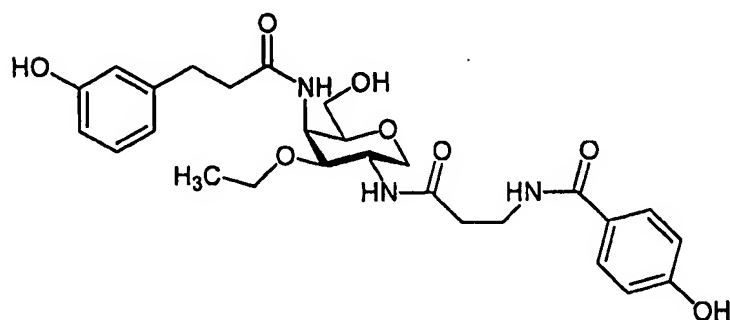
5



10  $\delta_H$  (400 MHz;  $CDCl_3$ ) 1.01 (3 H, t,  $J$  7.0 Hz), 2.49 (2H expected), 2.95 (1 H, t,  $J$  10.9 Hz), 3.30-3.80 (6 H expected), 3.90 (1 H, m), 4.00 (1 H, dd,  $J$  10.6 Hz and  $J$  5.4 Hz), 4.63 (1 H, br. s), 4.75 (1 H, dd,  $J$  9.4 Hz and  $J$  3.4 Hz), 6.00 (1 H, d,  $J$  6.4 Hz), 6.16 (1 H, t,  $J$  5.8 Hz), 7.55 (1 H, t,  $J$  7.8 Hz), 8.02 (2 H, t,  $J$  6.4 Hz), 8.25 (1 H, d,  $J$  10.0 Hz) and 8.33 (1 H, d,  $J$  1.2 Hz).

**Compound 200**

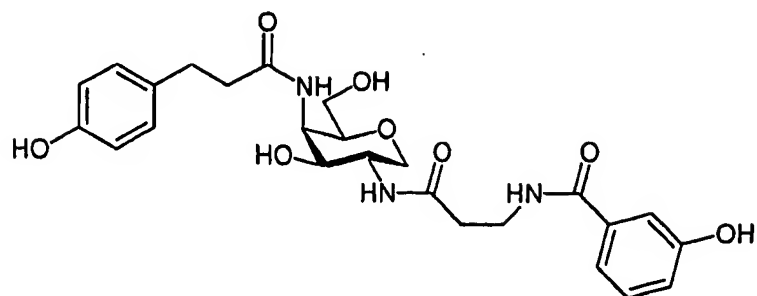
15



20  $\delta_H$  (400 MHz;  $CDCl_3$ ) 0.94 (3 H, t,  $J$  7.0 Hz), 1.07 (2 H, t,  $J$  6.8 Hz), 2.30-2.40 (4 H expected), 2.49 (2 H expected), 2.60-3.00 (4 H expected), 3.30-3.85 (4 H expected), 3.91-4.10 (2 H, m), 4.44 (1 H, dd,  $J$  9.8 Hz and  $J$  4.2 Hz), 4.49 (1 H, br. s), 6.57 (2 H, m), 6.75 (2 H, dd,  $J$  8.6 Hz and  $J$  1.8 Hz), 7.02 (1 H, t,  $J$  7.7 Hz), 7.66 (2 H, d,  $J$  8.4 Hz), 7.78 (2 H, dd,  $J$  14.8 Hz and  $J$  8.4 Hz), 8.22

(1 H, q,  $J$  11.6 Hz and  $J$  5.6 Hz), 9.2 (1 H, s) and 9.94 (1 H, d,  $J$  9.2 Hz).

**Compound 159**

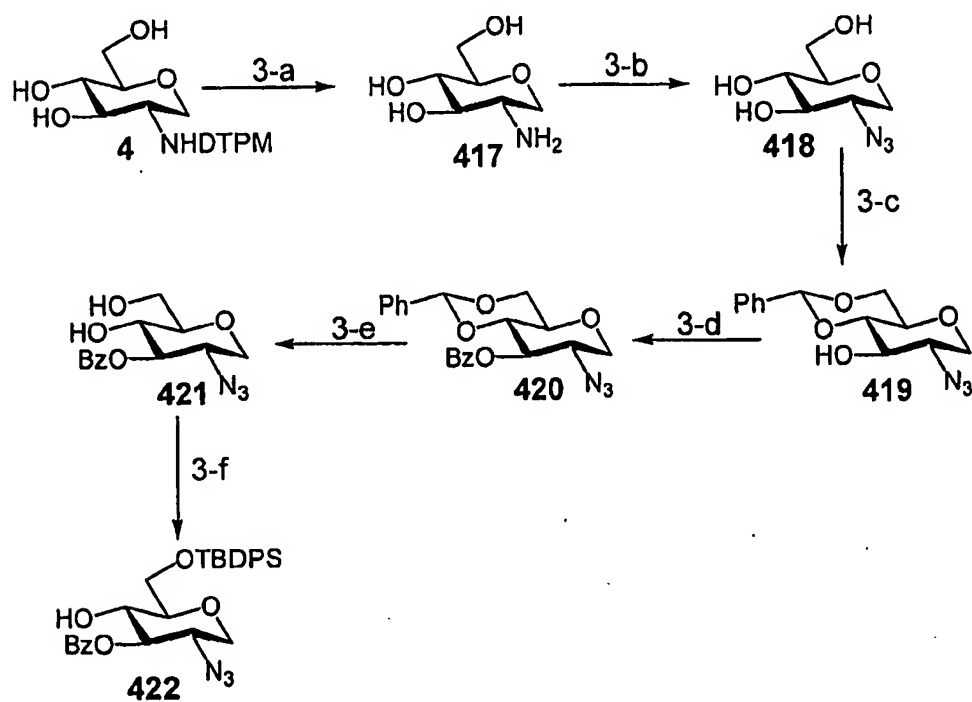


5

$\delta_H$  (400 MHz;  $CDCl_3$ ) 2.30-2.90 (6 H expected), 3.05-3.46 (7 H expected), 3.59 (2 H, m), 3.80 (2 H, m), 3.93 (1 H, m), 4.21 (1 H, dd,  $J$  8.8 Hz and  $J$  4.4 Hz), 4.49 (1 H, t,  $J$  6.0 Hz), 4.77 (1 H, d,  $J$  4.8 Hz), 6.64 (1 H, dd,  $J$  6.4 Hz and  $J$  2.0 Hz), 6.87 (1 H, m), 6.98 (2 H, dd,  $J$  8.6 Hz and  $J$  2.6 Hz), 7.20 (2 H, dt,  $J$  5.4 Hz and  $J$  2.2 Hz), 7.74 (1 H, dd,  $J$  20.4 Hz and  $J$  9.2 Hz), 8.34 (1 H, t,  $J$  5.6 Hz), 9.11 (1 H, d,  $J$  11.6 Hz) and 9.60 (1 H, br. s).

10

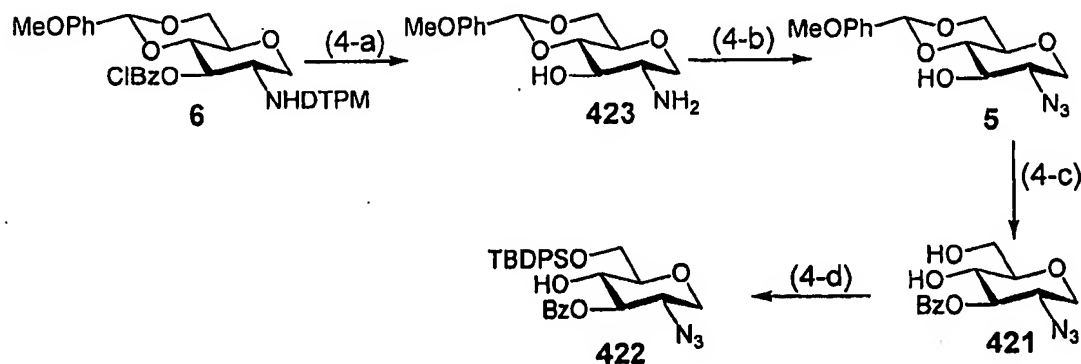
Example 3: Synthesis of a 1,5-anhydro-2-azido-3-O-benzoyl-6-O-(t-butyldiphenylsilyl)-2-deoxy-D-glucitol.



5

3-a. General Method 8; 3-b. General Method 17; 3-c. General Method 4; 3-d. General Method 5; 3-e. General method 18; 3-f. General Method 19.

Example 4: Synthesis of a 1,5-anhydro-2-azido-3-O-benzoyl-6-O-(t-butyl-diphenylsilyl)-2-deoxy-D-glucitol.



5

4-a. O- and N- Deprotection of Glucitol Building Block 6 to form Glucitol 423.

Compound **423** was synthesised according to General Method 16, 87.2% yield (0.837g).  $[M+H]^+ = 282.30$ ; 98% Purity by ELSD.

10 4-b. Formation of 2-Deoxy-2-Azido Glucitol Building Block 5 from Building Block 423.

The formation of building block **5** was carried out according to the procedure described in General Method 17;  $[M+H]^+ = 308.1$ ; 98% purity by ELSD.

$R_t = 4.62$  mins (Agilent SB Zorbax C18 4.6 x 50mm (5 $\mu$ m, 80Å), LC Mobile

15 Phase: Acetonitrile : Water 0.1% formic acid). Gradient as follows:

| Time (min) | water% | CH <sub>3</sub> CN% | Flow ml/min |
|------------|--------|---------------------|-------------|
| 0.00       | 90.0   | 10.0                | 1.500       |
| 1.00       | 90.0   | 10.0                | 1.500       |
| 7.00       | 0.0    | 100.0               | 1.500       |
| 20 12.00   | 0.0    | 100.0               | 1.500       |
| 20.00      | 0.0    | 100.0               | 1.500       |

4-c. Preparation of Building Block 421 from Building Block 5 in Three Steps.

Compound **421** was subjected to conditions as described in General Method 18. Then the product of this reaction was directly subjected to the conditions as described in General Method 3. Finally the material was subjected to the conditions as described in General Method 19 to provide **5** as a white solid in

69% yield after purification;  $[M+H]^+ = 294.6$ .

Rt = 3.52 mins, (Agilent SB Zorbax C18 4.6 x 50mm (5 $\mu$ m, 80Å) LC Mobile

Phase: Acetonitrile : Water 0.1% formic acid) Gradient as follows;

|    | Time(min) | water% | CH <sub>3</sub> CN% | Flow ml/min |
|----|-----------|--------|---------------------|-------------|
| 5  | 0.00      | 90.0   | 10.0                | 2.00        |
|    | 1.00      | 90.0   | 10.0                | 2.00        |
|    | 7.00      | 0.0    | 100.0               | 2.00        |
|    | 12.00     | 0.0    | 100.0               | 2.00        |
|    | 13.00     | 90.0   | 10.0                | 2.00        |
| 10 | 15.00     | 90.0   | 10.0                | 2.00        |

#### 4-d. Silyl Protection of Building Block 421 to form Building Block 422

Compound 422 was formed according to the procedure described in General

Method 19 in 87% yield,  $[M+H]^+ = 532.3$ ; 100% purity by ELSD

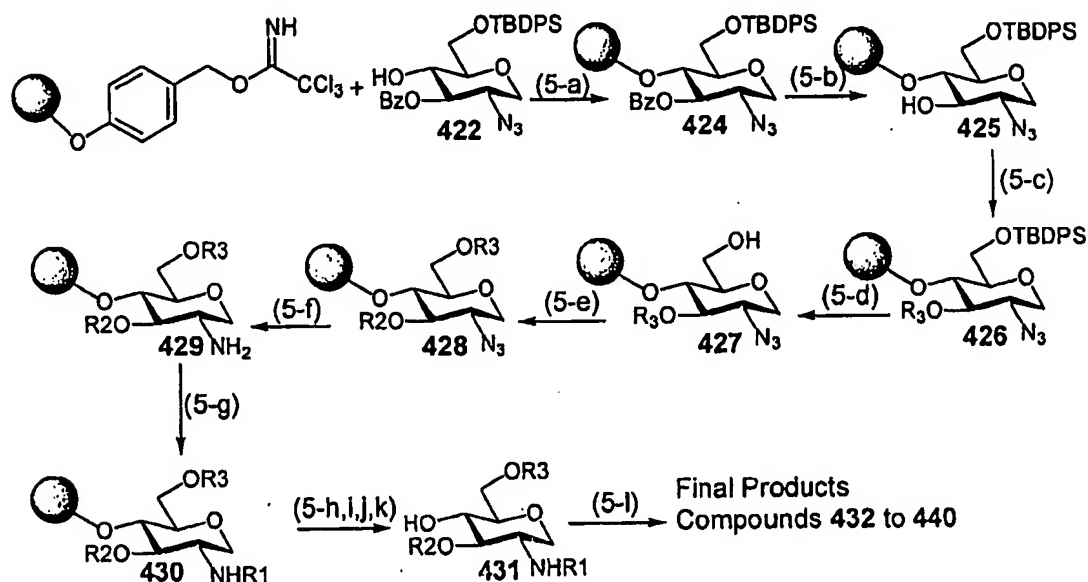
15 Rt = 6.84 mins, (Agilent SB Zorbax C18 4.6 x 50mm (5 $\mu$ m, 80Å) LC Mobile

Phase: Acetonitrile : Water 0.1% formic acid) Gradient as follows:

|    | Time(min) | water% | CH <sub>3</sub> CN% | Flow ml/min |
|----|-----------|--------|---------------------|-------------|
| 20 | 0.00      | 90.0   | 10.0                | 2.00        |
|    | 1.00      | 90.0   | 10.0                | 2.00        |
|    | 7.00      | 0.0    | 100.0               | 2.00        |
|    | 14.00     | 0.0    | 100.0               | 2.00        |
|    | 15.00     | 90.0   | 10.0                | 2.00        |

25 Spectral analysis for compound 422; <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400MHz): 0.99 (s, 9 H), 2.99 (d, *J* = 3.76Hz, 1 H), 3.21 (t, *J* = 11.1, 11.5 Hz, 1 H), 3.31 - 3.34 (m, 1 H), 3.65-3.72 (m, 1 H), 3.75-3.82 (m, 1 H), 3.82 – 3.89 (m, 2 H), 4.02 (dd, *J* = 5.4, 11.5 Hz, 1 H), 5.11 (t, *J* = 9.2, 9.7 Hz, 1 H), 7.28-7.43 (m, 8 H), 7.51-7.55 (m, 1 H), 7.58-7.56 (m, 2 H), 8.02-8.06 (m, 2 H).

Example 5: General synthetic route for preparation of a Library of Glucitol Peptide Mimetics.



- 5 5-a. Coupling of Glucitol Building Block 422 to the Trichloroacetimidate Derivatised Wang Resin to provide 424.

Building Block-Resin Conjugate was prepared according to the procedure outlined in General Method 20.

- 10 5-b. Removal of the Benzoyl Group to Form 425.

Compounds represented by no. 424 were prepared according to General Method 21.

- 15 5-c. Alkylation at position 3 of Conjugate 425 to Provide Resin-Building Block 426.

The compounds represented by no. 425 were subjected to the conditions as described in General Method 22 to provide compounds no. 426.

5-d. Removal of TBDPS group

- 20 The resins designated by 426 were subjected to the conditions as described in General Method 23.

5-e. Alkylation at position 6 to provide



The resin bound compounds designated by 427 were alkylated in groups as described for General Method 22.

5-f. Reduction of Azido group to provide

- 5 The resin bound compounds designated by 428 were subjected to the conditions as described in General Method 24.

5-g. N-Acylations

- 10 The resins designated by 429 were either subjected to the conditions as described in General Method 25: *Method 1*, or, were subjected to the conditions as described in General Method 22: *Method 2*.

5-h. Reduction of the Nitro Group

- 15 *If required*, the substituent nitro group of a side-arm was reduced to the amine according to the procedure described in General Method 26.

5-i. Deprotection of the Fmoc Protecting Group

- 20 *If required*, the Fmoc protecting group on side-arms was deprotected according to the procedure described in General Method 27.

5-j. Guanylation of amino group

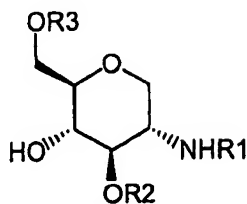
*If required*, amino group substituents of side-arms were guanylated according to the procedure described in General Method 28.

25 5-k. Cleavage of final products from the resins

The final products were cleaved from resin according to the procedure described in General Methods 29. Final compounds were purified by HPLC-MS (See Table 4).

30 5-l. Hydrolysis of Me ester

*If required*, the cleavage mixtures designated by 431 were individually treated with a solution of LiOH (0.5 molar) in MeOH/water (1/1) (ph~14) for a week. The solvents were removed in vacuo and the residue was purified by HPLC.

**Table 4: Library of Glucitol compounds**

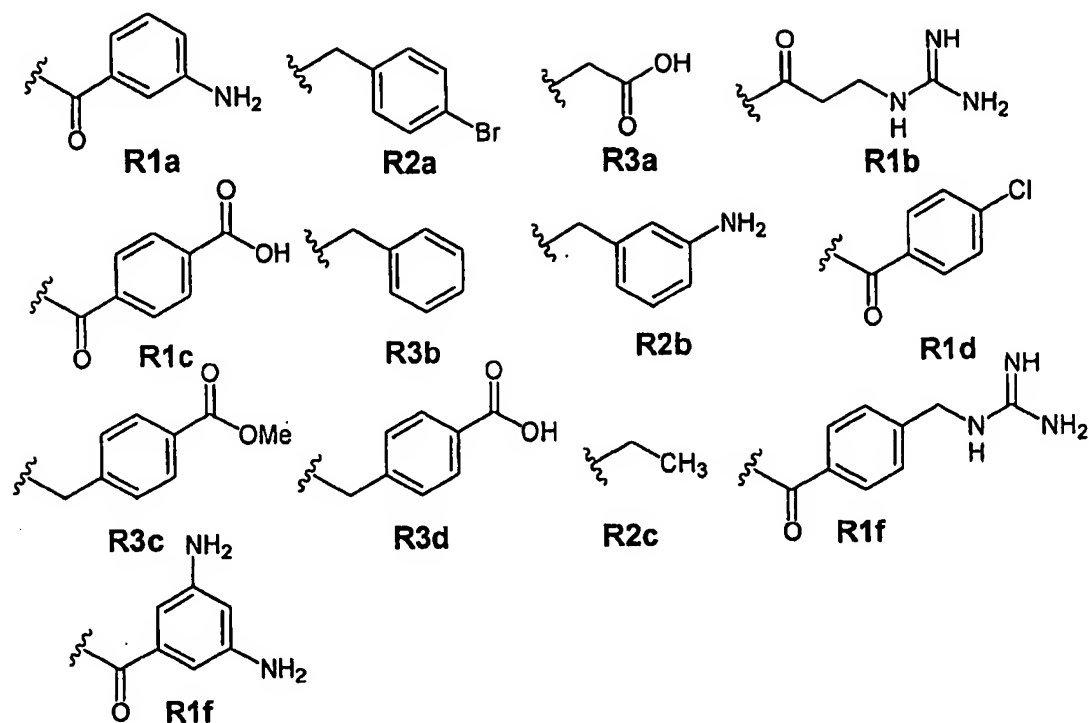
5

| Comp. No. | R1  | R2  | R3  | M+H   | Purity <sup>1</sup> (%) | Rt   | Yield mg | Yield <sup>2</sup> % |
|-----------|-----|-----|-----|-------|-------------------------|------|----------|----------------------|
| 432       | R1a | R2a | R3a | 509.1 | 85.8 ELSD               | 3.71 | 14.1     | 53.9                 |
| 433       | R1c | R2b | R3b | 507.2 | 63.6 UV                 | 3.38 | 4.9      | 18.7                 |
| 434       | R1d | R2b | R3c | 555.2 | 77.9UV                  | 4.04 |          | 14.1                 |
| 435       | R1d | R2b | R3d | 541.1 |                         | 3.62 | 8.6      | 30.9                 |
| 436       | R1a | R2c | R3a | 369.1 | 73.2 ELSD               | 0.86 | 9.6      | 50.5                 |
| 437       | R1b | R2c | R3c | 453.2 | 80-UV                   | 3.18 |          |                      |
| 438       | R1b | R2c | R3d | 439.1 |                         | 2.52 | 1.6      | 7.1                  |
| 439       | R1e | R3b | R3a | 487.1 | 63.8-UV                 | 2.55 | 12.9     | 51.6                 |
| 440       | R1f | R3b | R3a | 446.1 | 65-UV                   | 2.39 | 3.6      | 15.7                 |

<sup>1</sup>UV implies purity by Ultra-Violet detection, ELSD implies purity by Electron Light Scattering Detection.

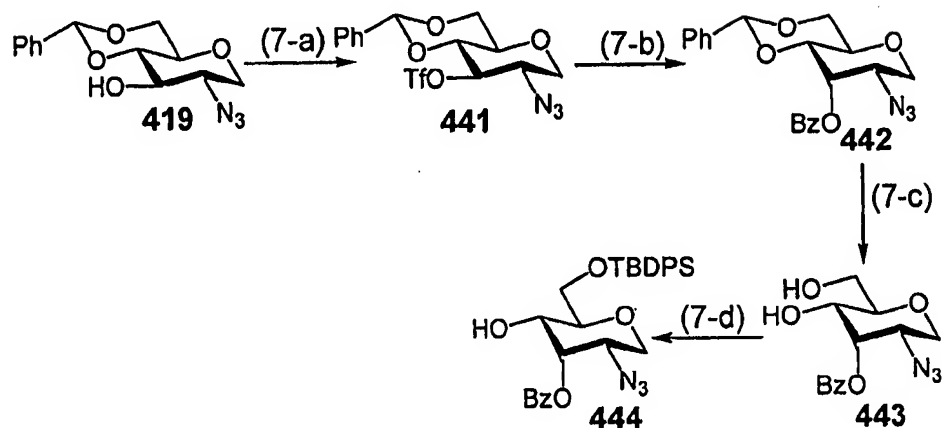
<sup>2</sup>Yield calculated for the whole solid phase sequence; 140mg of resin was used for preparation of each compound; the substitution was 0.368mmol/g, thus the amount of the starting material was 0.0515mmol.

10

Side Chains for Table 4:5 HPLC Method for Compounds in Table 4:(Agilent SB Zorbax C18 4.6 x 50mm (5 $\mu$ m, 80Å) LC Mobile Phase:

Acetonitrile : Water 0.1% formic acid) Gradient as follows:

|    | Time(min) | water% | CH <sub>3</sub> CN% | Flow ml/min |
|----|-----------|--------|---------------------|-------------|
|    | 0.00      | 95.0   | 5.0                 | 2.00        |
| 10 | 1.00      | 95.0   | 5.0                 | 2.00        |
|    | 7.00      | 0.0    | 100.0               | 2.00        |
|    | 12.00     | 0.0    | 100.0               | 2.00        |
|    | 13.00     | 95.0   | 5.0                 | 2.00        |
|    | 15.00     | 95.0   | 5.0                 | 2.00        |

Example 7: Allitol Building Block Synthesis5 7-a. Synthesis of a 3-O-Triflate Glucitol 441.

Compound **419** (300 mg, 1.08 mmol) and symmetric collidine (0.22 mL, 1.65 mmol) were dissolved in anhydrous DCM (7.0 mL) and the solution then cooled to -25°C. A solution of trifluoromethanesulphonic anhydride (0.27 mL, 1.65 mmol) in DCM (2.77 mL) was injected into the solution and the reaction  
 10 allowed to proceed overnight. The solution was reduced to dryness, the residue dissolved in DCM (15 mL) and then washed with 0.5 molar HCl. The organic phase was dried over MgSO<sub>4</sub>, filtered and the solvent removed in vacuo to provide the product **441** (399 mg, 90.3%).

15 7b. Inversion at the C-3 position of a Glucitol Block to Form Allitol Block 442.

To a solution of compound **441** (4.089 mmol) in DMF (7 mL) was added a solution of LiOBz (1.794 mmol) in DMF (7 mL). The reaction was allowed to proceed at room temperature overnight. The solvent was removed in vacuo and the resulting residue redissolved in EtOAc. The solution was then  
 20 washed with H<sub>2</sub>O, the organic layer was collected, dried over MgSO<sub>4</sub>, filtered and the solvent removed in vacuo to provide allitol block **442** (74.1% yield).

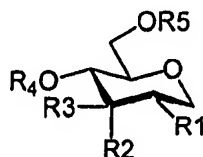
7c. Cleavage of the Benzylidene Ring System to Provide Allitol Block 443.

Compound **443** was prepared according to the procedure as described in  
 25 General Method 18.

7d. Formation of the Differentially Protected 1,5-Anhydro Allitol Building Block  
Compound **444** was prepared according to the procedure as described by General Method 19.

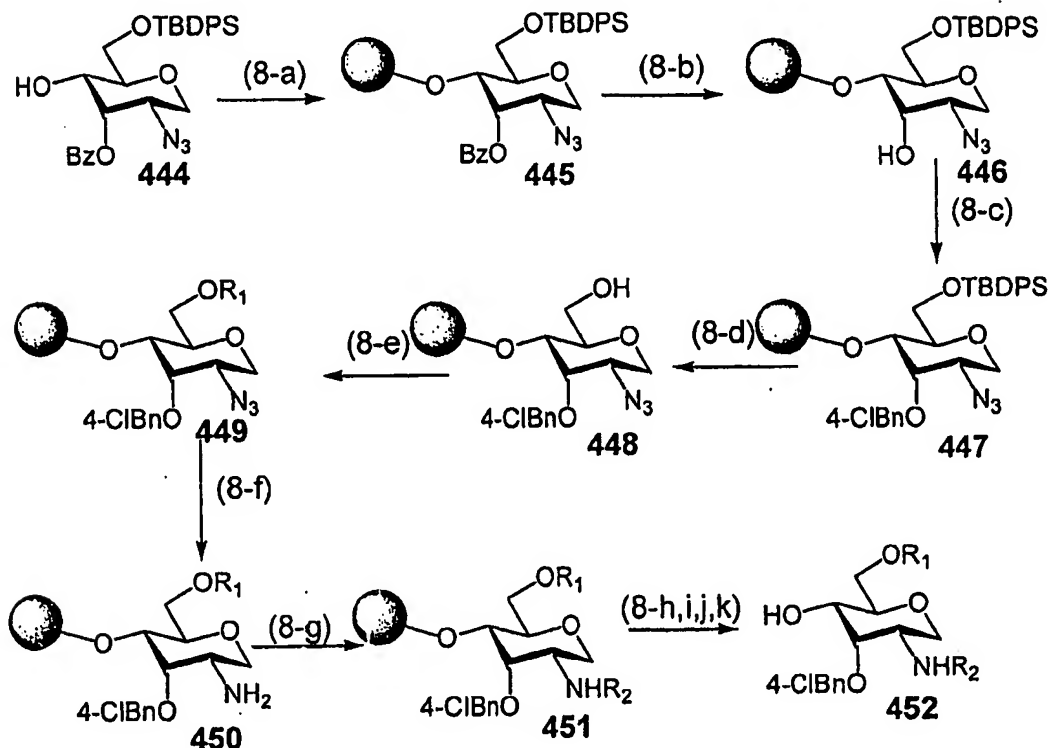
5

Table 5: Analytical Data for Intermediates and Final Compound in the Synthesis of Allitol Building Block **444**.



10

| Comp.      | R1             | R2  | R3  | R4          | R5    | Observed.<br>Mass + H |
|------------|----------------|-----|-----|-------------|-------|-----------------------|
| <b>441</b> | N <sub>3</sub> | H   | OTf | Benzyldiene |       | 410.13                |
| <b>442</b> | N <sub>3</sub> | OBz | H   | Benzyldiene |       | 382.15                |
| <b>443</b> | N <sub>3</sub> | OBz | H   | H           | H     | 294.12                |
| <b>444</b> | N <sub>3</sub> | OBz | H   | H           | TBDPS | 532.15                |

Example 8: Prototype Library using H-Allose Building Block

- 5 8-a. Coupling of Allitol Building Block **444** to the Trichloroacetimidate Derivatised Wang Resin to provide **445**.

Building Block-Resin Conjugate was prepared according to the procedure outlined in General Method 20.

- 10 8-b. Removal of the Benzoyl Group to Form **446**.

Compound **446** was prepared from precursor **445** according to General Method 21.

- 15 8-c. Alkylation at position 3 of Conjugate **446** to Provide Resin-Building Block **447**.

The compound represented by **446** were subjected to the conditions as described in General Method 22 to provide compounds no. **447**.

8-d. Removal of TBDPS group

- 20 The resins designated by **447** were subjected to the conditions as described

in General Method 23.

8-e. Alkylation at position 6

The resin bound compounds designated by 448 were alkylated in groups as  
5 described for General Method 22.

8-f. Reduction of Azido group

The resin bound compounds designated by 449 were subjected to the  
conditions as described in General Method 24.

10

8-g. N-Acylation

The resins designated by 450 were either subjected to the conditions as  
described in General Method 25: *Method 1*, or, were subjected to the  
conditions as described in General Method 25: *Method 2*.

15

8-h. Reduction of the Nitro Group

*If required*, the substituent nitro group of a side-arm was reduced to the  
amine according to the procedure described in General Method 26.

20 8-i. Deprotection of the Fmoc Protecting Group

*If required*, the Fmoc protecting group on side-arms was deprotected  
according to the procedure described in General Method 27.

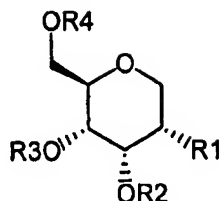
8-j. Guanylation of amino group

25 *If required*, amino group substituents of side-arms were guanylated according  
to the procedure described in General Method 28.

8-k. Cleavage of final products from the resins (14-final product)

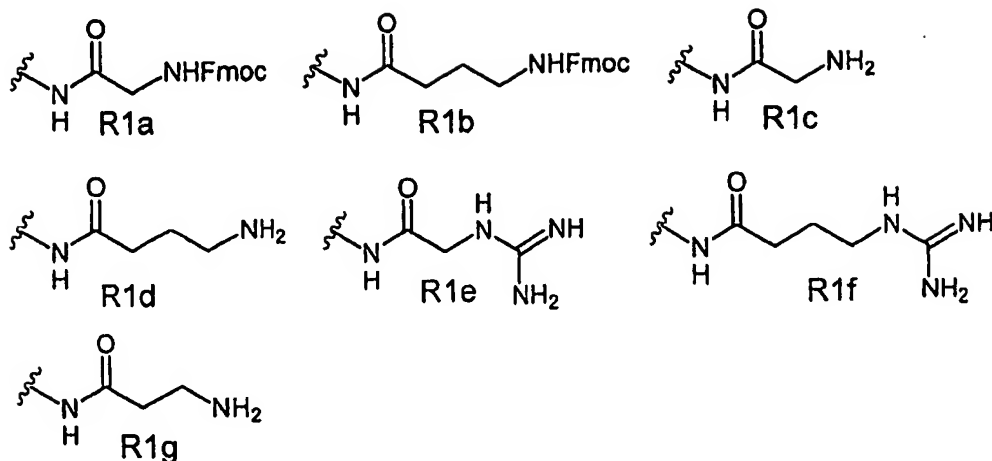
The final products were cleaved from resin according to the procedure  
30 described in General Methods 29 to provide compounds designated by no.  
452. Final compounds were purified by HPLC-MS.

Table 6: Structural and Analytical Data for Allitol Based Building Block

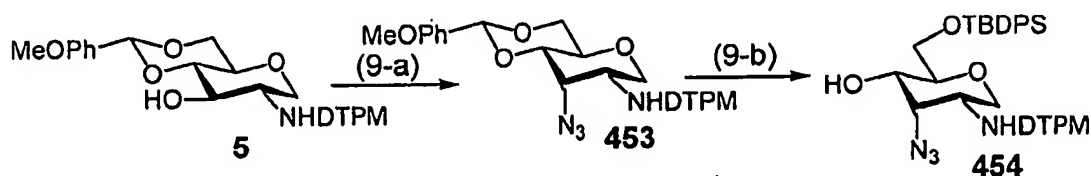
Intermediates and Final Products

| Compound | R1              | R2         | R3 | R4           | Exp. Mol M+H |
|----------|-----------------|------------|----|--------------|--------------|
| 453      | N <sub>3</sub>  | Bz         | H  | TBDPS        | 532.27       |
| 454      | N <sub>3</sub>  | H          | H  | TBDPS        | 428.20       |
| 455      | N <sub>3</sub>  | p-Clbenzyl | H  | TBDPS        | 552.25       |
| 456      | N <sub>3</sub>  | p-Clbenzyl | H  | H            | 314.1        |
| 457      | N <sub>3</sub>  | p-Clbenzyl | H  | p-ClBenzyl   | No Data      |
| 458      | N <sub>3</sub>  | p-Clbenzyl | H  | 2-Naphthyl   | 454.27       |
| 459      | NH <sub>2</sub> | p-Clbenzyl | H  | p-ClBn       | 412.20       |
| 460      | NH <sub>2</sub> | p-Clbenzyl | H  | 2-Naphthyl   | 428.20       |
| 461      | R1a             | p-Clbenzyl | H  | p-ClBn       | 691.40       |
| 462      | R1a             | p-Clbenzyl | H  | 2-Naphthyl   | 707.40       |
| 463      | R1a             | p-Clbenzyl | H  | 4-MeBiphenyl | 733.42       |
| 464      | R1b             | p-Clbenzyl | H  | p-ClBn       | 719.40       |
| 465      | R1b             | p-Clbenzyl | H  | 2-Naphthyl   | 735.50       |
| 466      | R1b             | p-Clbenzyl | H  | 4-MeBiphenyl | 747.44       |
| 452a     | R1c             | p-Clbenzyl | H  | p-ClBn       | 469.26       |
| 452b     | R1c             | p-Clbenzyl | H  | 2-Naphthyl   | 485.32       |
| 452c     | R1d             | p-Clbenzyl | H  | p-ClBn       | 497.26       |
| 452d     | R1d             | p-Clbenzyl | H  | 2-Naphthyl   | 513.37       |
| 452f     | R1e             | p-Clbenzyl | H  | p-ClBn       | 511.28       |
| 452g     | R1e             | p-Clbenzyl | H  | 2-Naphthyl   | 527.33       |
| 452h     | R1f             | p-Clbenzyl | H  | p-ClBn       | 539.31       |
| 452i     | R1f             | p-Clbenzyl | H  | 2-Naphthyl   | 555.38       |
| 452j     | R1g             | p-Clbenzyl | H  | 4-Mebiphenyl | 525.30       |
| 452k     | R1c             | p-Clbenzyl | H  | 4-Mebiphenyl | 511.20       |



Sidearms for Table 6

5 Example 9: Synthesis of a 1,5-anhydro-3-azido-6-O-(t-butyl dimethylsilyl)-2,3-dideoxy-2-[(1,3-dimethyl-2,4,6-(1H, 3H, 5H)-trioxopyrimidin-5-ylidene)methylamino]-D-allitol.



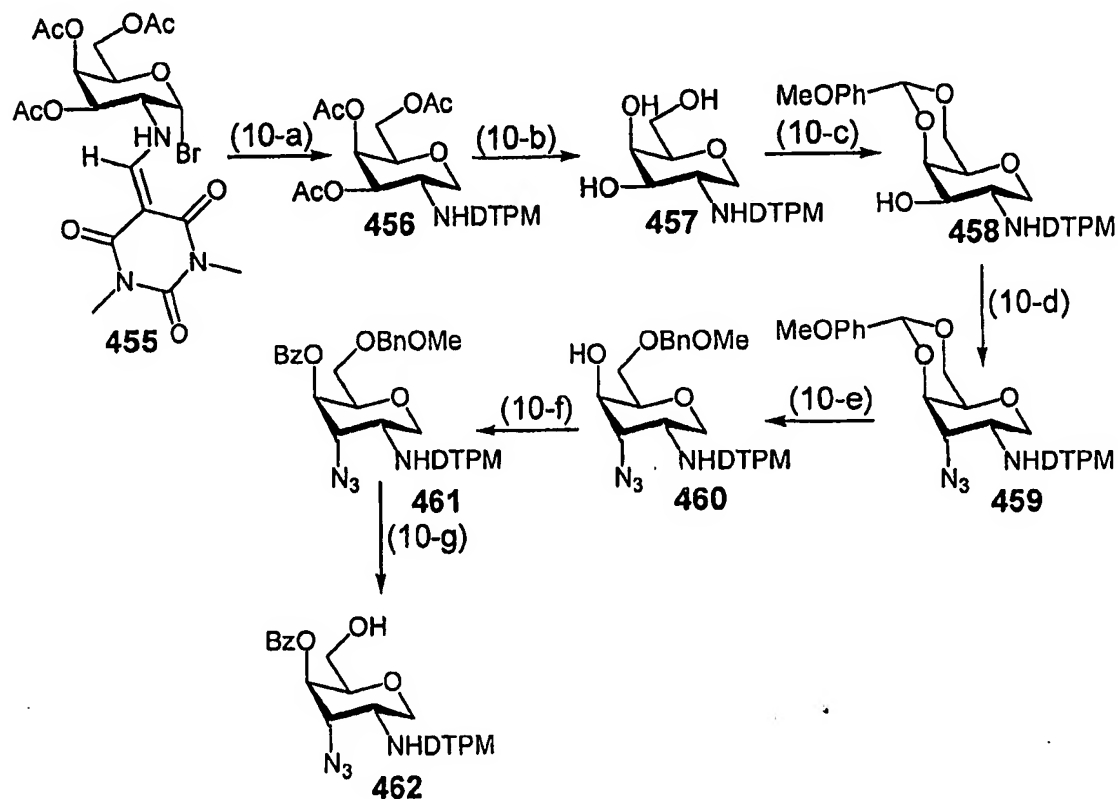
10 9-a. Formation of a Aminoallitol Building Block From a Glucitol Precursor.

Compound 5 was reacted according to the procedure described in General Method 6.

9-b. Formation of a Silyl Protected Building Block.

15 Compound 453 was reacted according to the procedure described in General Method 18. The product of this reaction was reacted according to the procedure described in General Method 19 to provide compound 454.

Example 10: Synthesis of a 1,5-anhydro-3-azido-4-O-benzoyl-2,3-dideoxy-2-[(1,3-dimethyl-2,4,6-(1H, 3H, 5H)-trioxypyrimidin-5-ylidene) methylamino]-6-O-(4-methoxybenzyl)--D-gulitol.



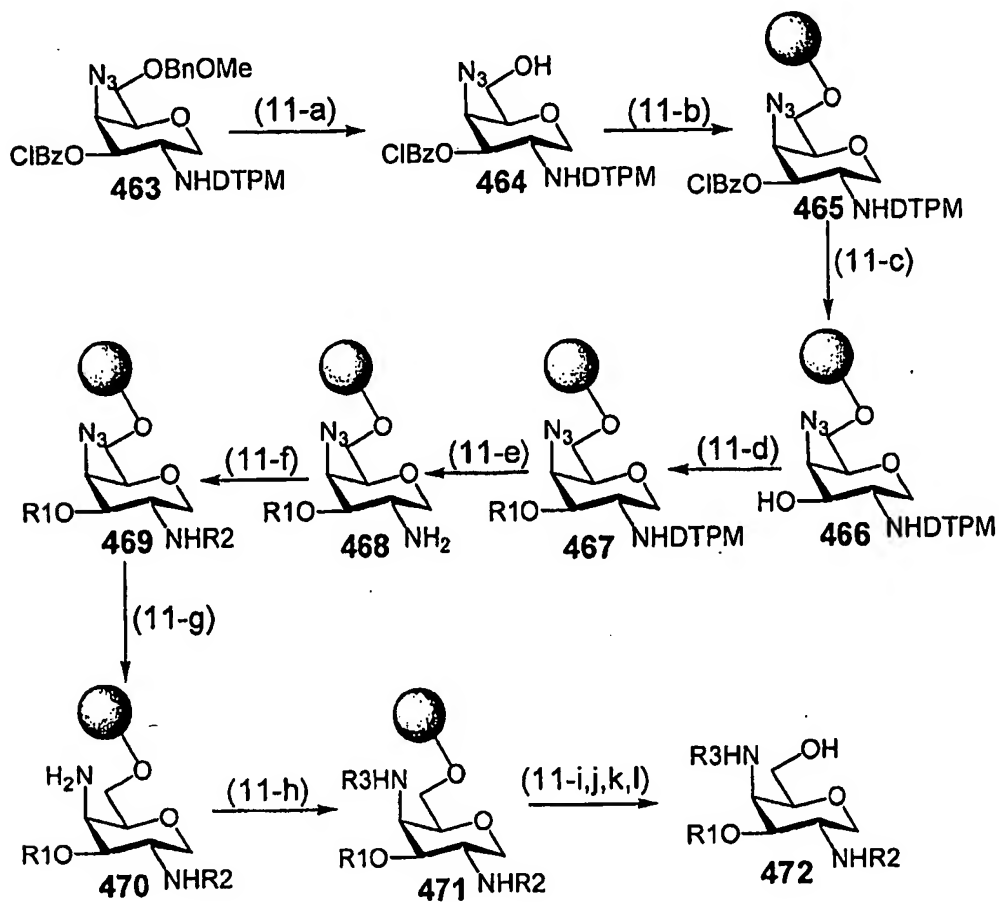
5

10-a. General Method 2; 10-b. General Method 3; 10-c. General Method 4;

10-d. General Method 6; 10-e. General Method 33; 10-f. General Method 5;

10 10-g. General Method 14.

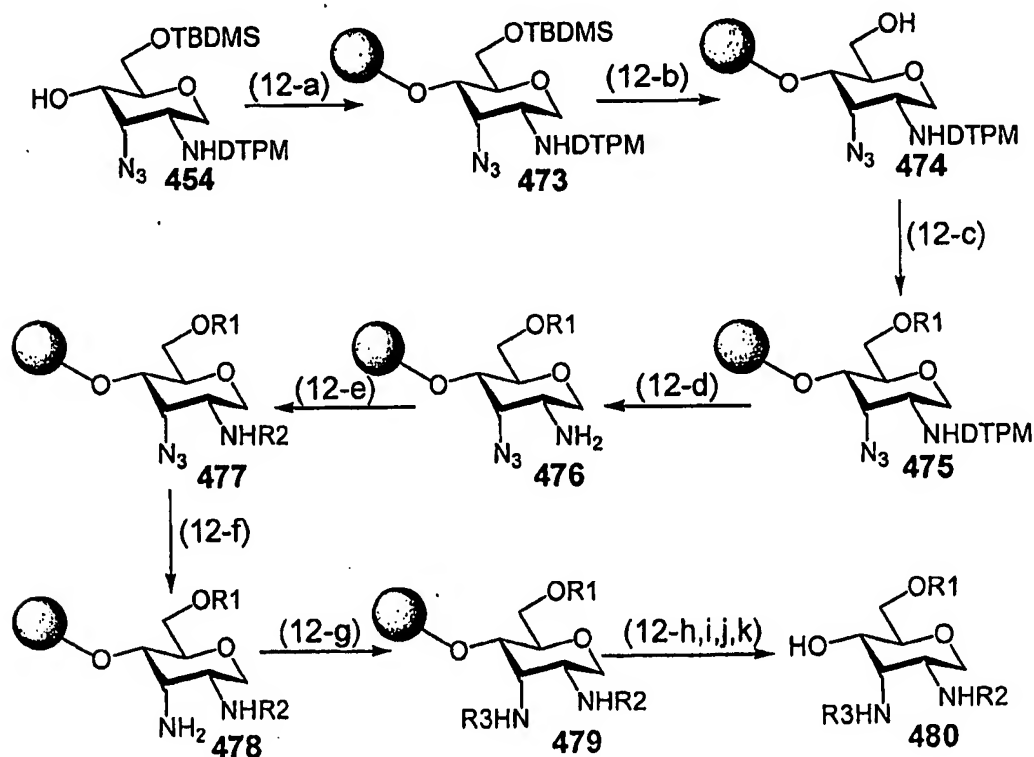
Example 11: Synthesis of a Library of Compounds by Solid Phase Techniques Using a Galactitol Building Block



5

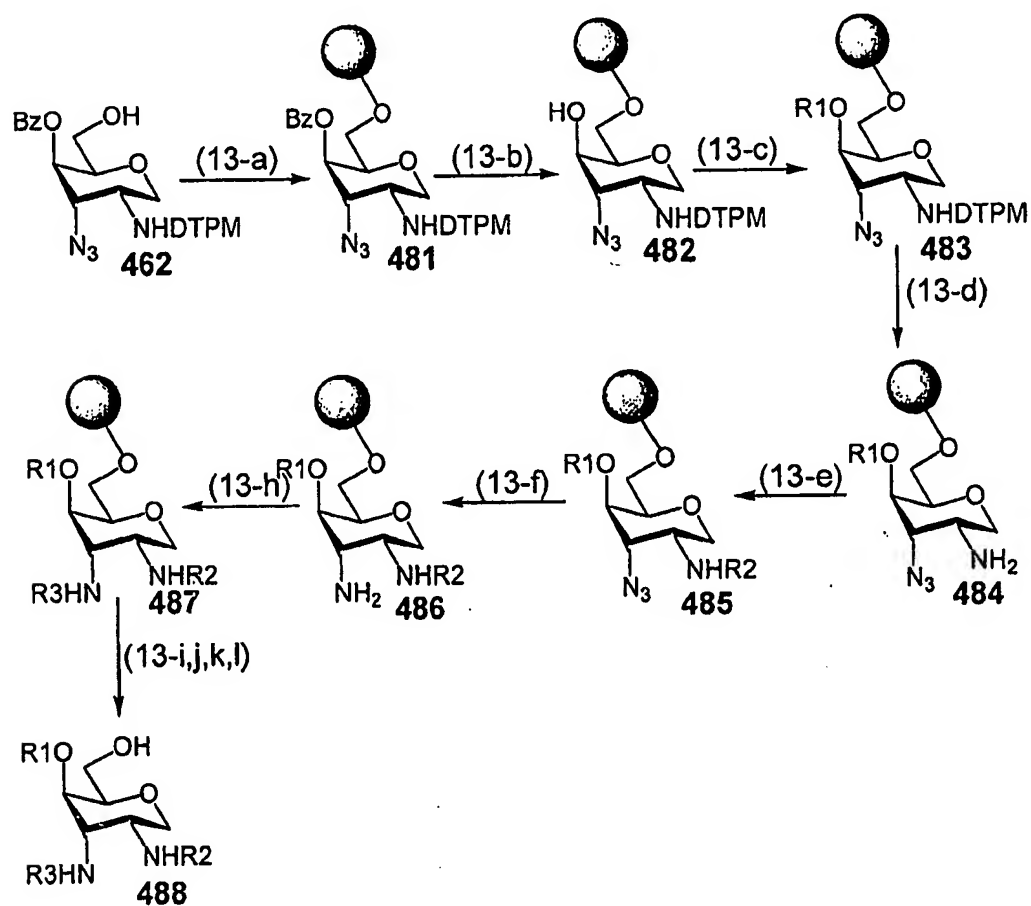
11-a. General Method 14; 11-b. General Method 20; 11-c. General Method 21; 11-d. General Method 22; 11-e. General Method 32; 11-f. General Method 25; 11-g. General Method 24; 11-h. General Method 25; 11-i to l selected from General Methods 26-29 (as appropriate).

10

Example 12: Solid Phase Synthesis of a 2,5-Bis Amino-Allitol Library.

- 5 12-a. General Method 20; 12-b. General Method 23; 12-c. General Method 22; 12-d. General Method 32; 12-e. General Method 25; 12-f. General Method 24; 12-g. General Method 25; 12-h to k selected from General Methods 26-29 (as appropriate).

**Example 13: Synthesis of a Library of Compound by Solid Phase Techniques**  
**Using a Diamino Gulitol Based Building Block**



5

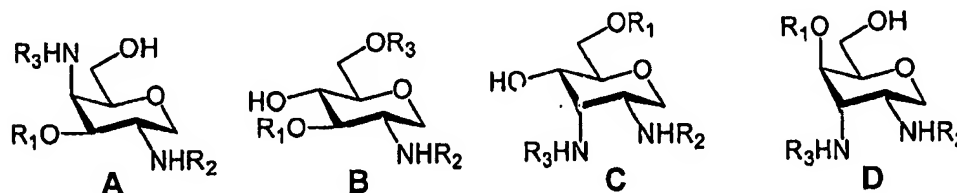
13-a. General Method 20; 13-b. General Method 21; 13-c. General Method 22; 13-d. General Method 31; 13-e. General Method 25; 13-f. General Method 24; 13-g. General Method 25; 13-h to k selected from General Methods 26-29 (as appropriate).

10

Example 14: Synthesis of an Exemplary Library 1

PART 1: In this example three different mimetics of three different peptide residues (ie. Phe mimetic 1, 2 and 3, Lys mimetic 1, 2 and 3, and Trp mimetic 1, 2 and 3<sup>s</sup>) maintain their position on the scaffold (Phe=R<sup>1</sup>, Lys=R<sup>2</sup>, Trp=R<sup>3</sup>), but the different mimetics are varied in relation to one another.

PART 2: further in this example, three different mimetics of three different peptide residues (ie. Phe mimetic 1, 2 and 3, Lys mimetic 1, 2 and 3, and Trp mimetic 1, 2 and 3<sup>s</sup>) are varied in their substitution point around the scaffold, ie. Phe mimetic 1 moves from R<sup>1</sup> to R<sup>2</sup> to R<sup>3</sup>, and so on.

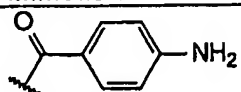
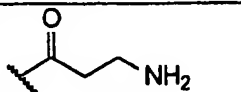
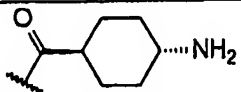
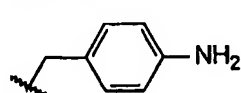
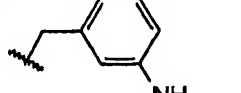
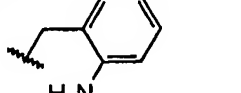
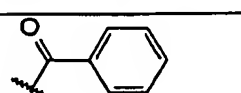
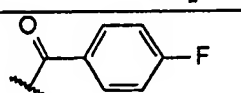
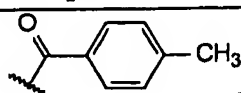
15 Table 8

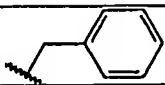
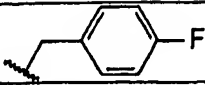
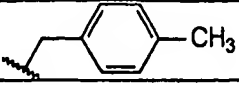
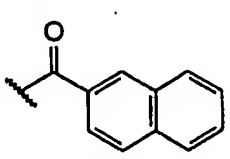
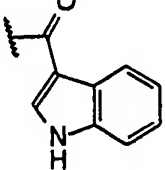
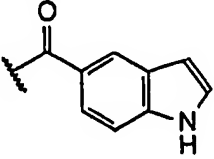
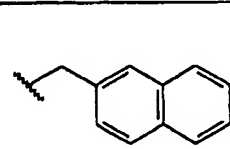
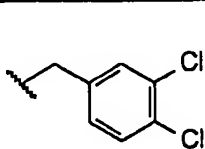
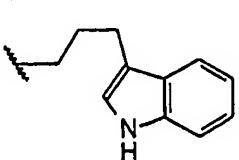
| R1            | R2            | R3            |
|---------------|---------------|---------------|
| PART 1        |               |               |
| Phe mimetic 1 | Lys mimetic 1 | Trp mimetic 1 |
| Phe mimetic 2 | Lys mimetic 1 | Trp mimetic 1 |
| Phe mimetic 3 | Lys mimetic 1 | Trp mimetic 1 |
| Phe mimetic 1 | Lys mimetic 1 | Trp mimetic 2 |
| Phe mimetic 2 | Lys mimetic 1 | Trp mimetic 2 |
| Phe mimetic 3 | Lys mimetic 1 | Trp mimetic 2 |
| Phe mimetic 1 | Lys mimetic 1 | Trp mimetic 3 |
| Phe mimetic 2 | Lys mimetic 1 | Trp mimetic 3 |
| Phe mimetic 3 | Lys mimetic 1 | Trp mimetic 3 |
| Phe mimetic 1 | Lys mimetic 2 | Trp mimetic 1 |
| Phe mimetic 2 | Lys mimetic 2 | Trp mimetic 1 |
| Phe mimetic 3 | Lys mimetic 2 | Trp mimetic 1 |
| Phe mimetic 1 | Lys mimetic 2 | Trp mimetic 2 |
| Phe mimetic 2 | Lys mimetic 2 | Trp mimetic 2 |
| Phe mimetic 3 | Lys mimetic 2 | Trp mimetic 2 |
| Phe mimetic 1 | Lys mimetic 2 | Trp mimetic 3 |
| Phe mimetic 2 | Lys mimetic 2 | Trp mimetic 3 |
| Phe mimetic 3 | Lys mimetic 2 | Trp mimetic 3 |
| Phe mimetic 1 | Lys mimetic 3 | Trp mimetic 1 |
| Phe mimetic 2 | Lys mimetic 3 | Trp mimetic 1 |
| Phe mimetic 3 | Lys mimetic 3 | Trp mimetic 1 |

|               |               |               |
|---------------|---------------|---------------|
| Phe mimetic 1 | Lys mimetic 3 | Trp mimetic 2 |
| Phe mimetic 2 | Lys mimetic 3 | Trp mimetic 2 |
| Phe mimetic 3 | Lys mimetic 3 | Trp mimetic 2 |
| Phe mimetic 1 | Lys mimetic 3 | Trp mimetic 3 |
| Phe mimetic 2 | Lys mimetic 3 | Trp mimetic 3 |
| Phe mimetic 3 | Lys mimetic 3 | Trp mimetic 3 |
| PART 2        |               |               |
| Lys mimetic 1 | Trp mimetic 1 | Phe mimetic 1 |
| Trp mimetic 1 | Phe mimetic 1 | Lys mimetic 1 |
| Lys mimetic 2 | Trp mimetic 1 | Phe mimetic 1 |
| Trp mimetic 1 | Phe mimetic 1 | Lys mimetic 2 |
| Lys mimetic 3 | Trp mimetic 1 | Phe mimetic 1 |
| Trp mimetic 1 | Phe mimetic 1 | Lys mimetic 3 |
| Lys mimetic 1 | Trp mimetic 2 | Phe mimetic 2 |
| Trp mimetic 2 | Phe mimetic 2 | Lys mimetic 1 |
| Lys mimetic 2 | Trp mimetic 2 | Phe mimetic 2 |
| Trp mimetic 2 | Phe mimetic 2 | Lys mimetic 2 |
| Lys mimetic 3 | Trp mimetic 2 | Phe mimetic 2 |
| Trp mimetic 2 | Phe mimetic 2 | Lys mimetic 3 |
| Lys mimetic 1 | Trp mimetic 3 | Phe mimetic 3 |
| Trp mimetic 3 | Phe mimetic 3 | Lys mimetic 1 |
| Lys mimetic 2 | Trp mimetic 3 | Phe mimetic 3 |
| Trp mimetic 3 | Phe mimetic 2 | Lys mimetic 2 |
| Lys mimetic 3 | Trp mimetic 3 | Phe mimetic 3 |
| Trp mimetic 3 | Phe mimetic 3 | Lys mimetic 3 |

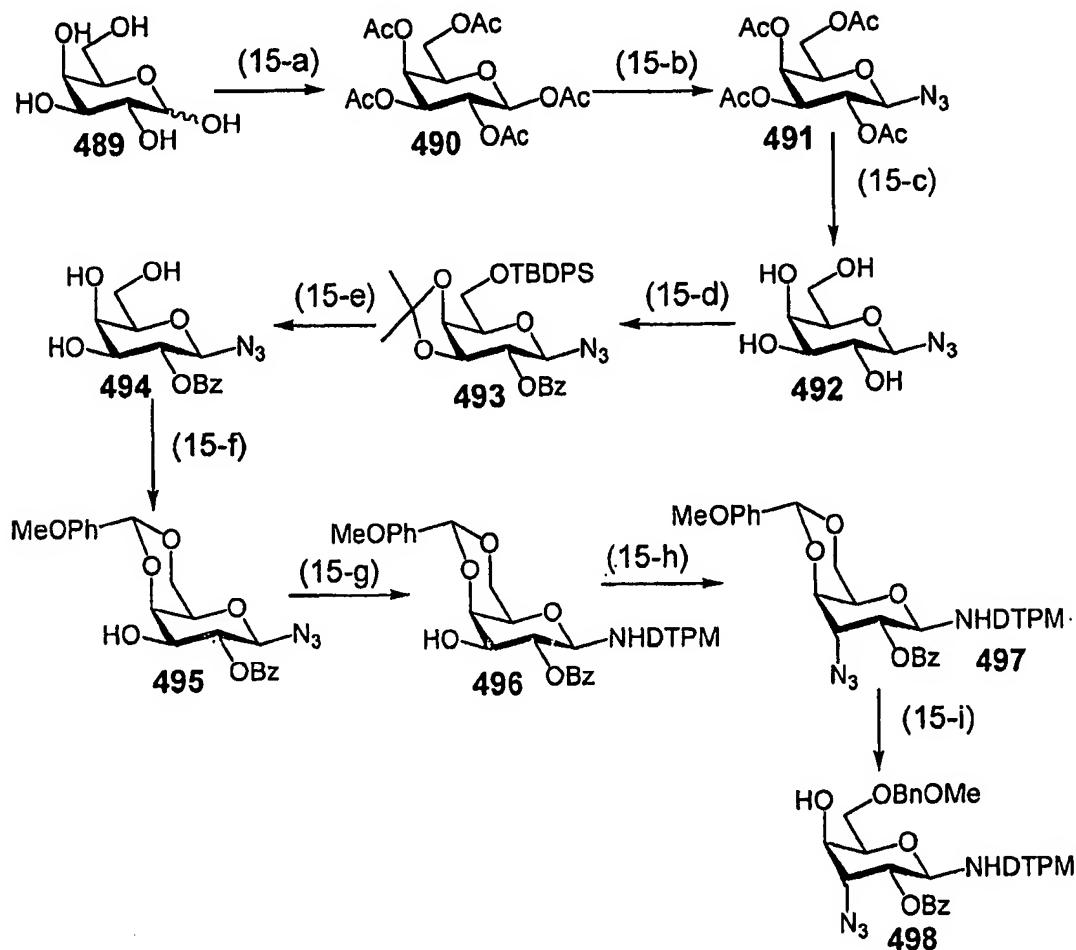
§The various scaffold substituents Lys, Phe, and Trp mimetics 1,2 and 3, are listed in Table 3 below. It is noted that in some case amine protection is required, which is typically effected by Boc protection. It is further noted that in some cases an O-linked mimetic is required and in other cases an N-linked mimetic is required. In the cases of the O-linked Lys mimetics, the mimetic is coupled as either the para, ortho or meta nitrobenzyl derivative and subsequently reduced to the amine.

10 Table 9

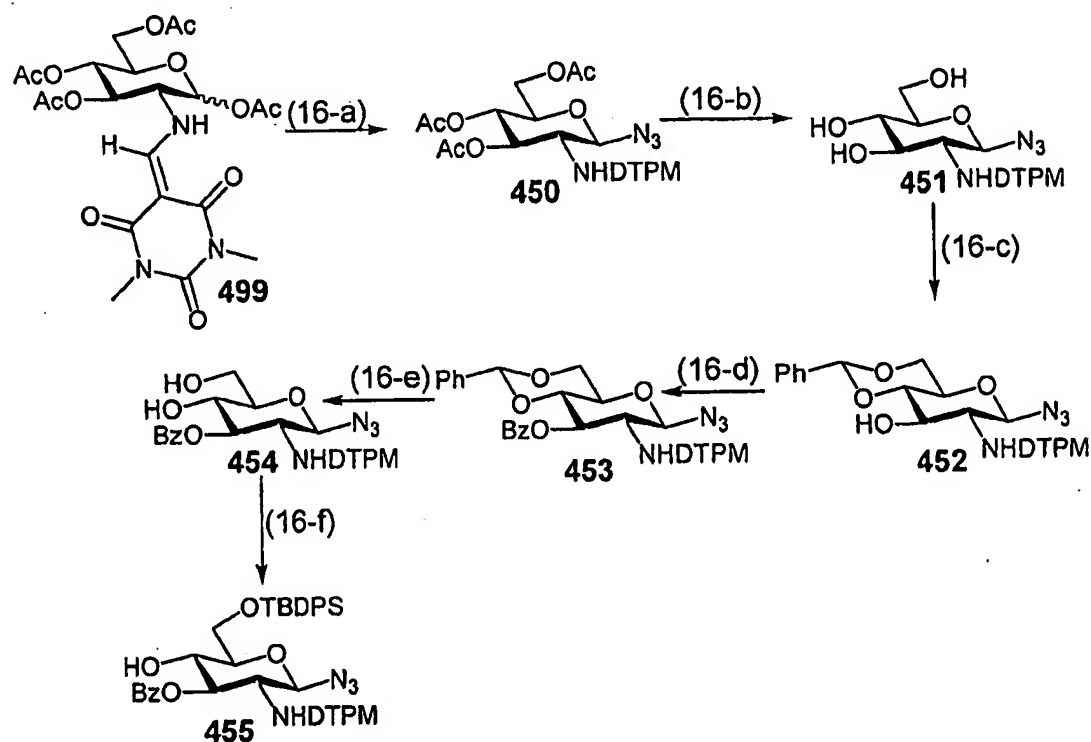
|                | Mimetic 1   | Mimetic 2  | Mimetic 3   |
|----------------|---|--|---|
| Lys (N-linked) |  |  |  |
| Lys (O-linked) |  |  |  |
| Phe (N-linked) |  |  |  |

|                |   |  |   |
|----------------|---|--|---|
| Phe (O-linked) |  |  |  |
| Trp (N-linked) |  |   |  |
| Trp (O-linked) |  |  |  |

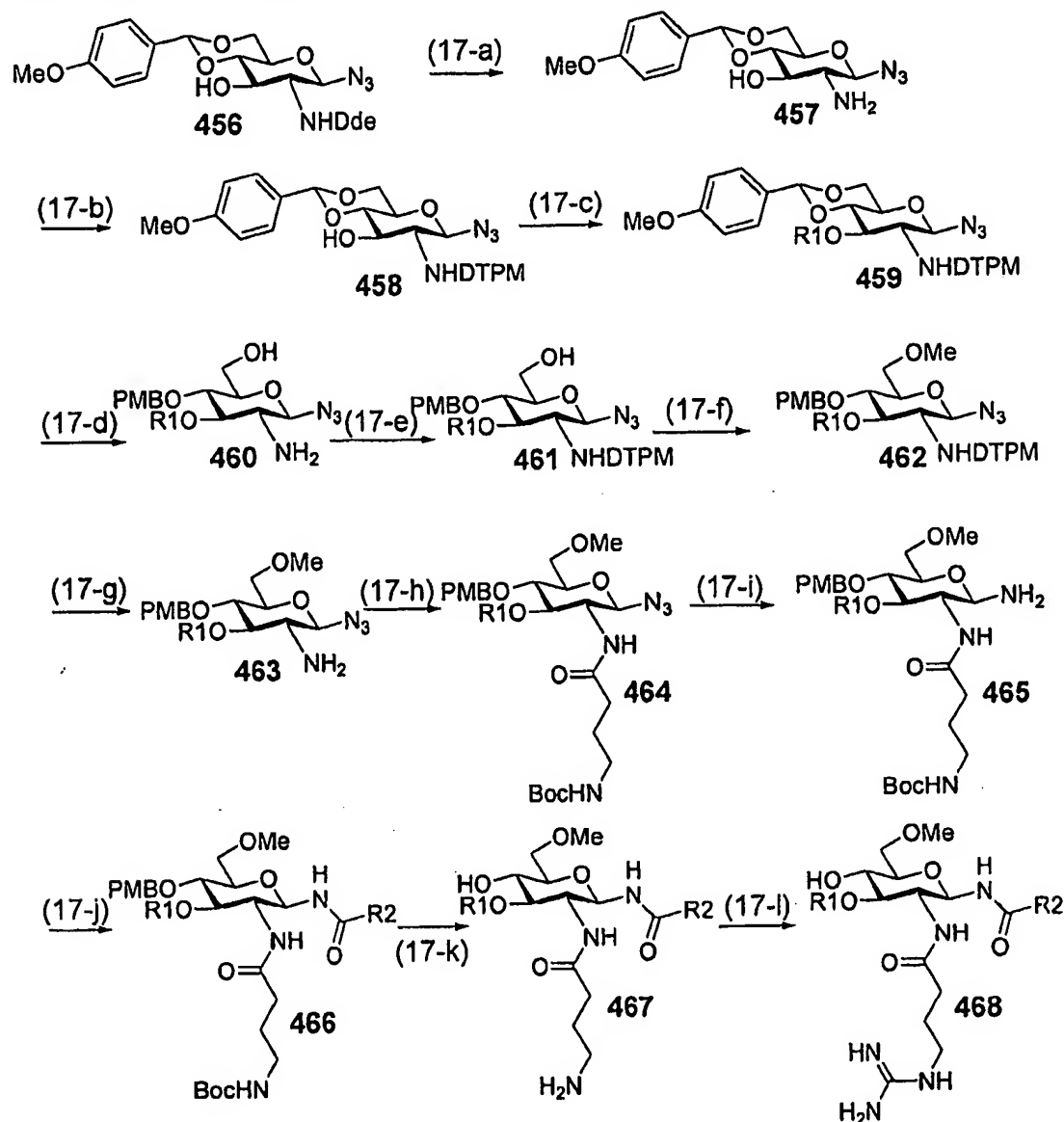


Example 15: A Gulitol N-Glycoside Building Block

- 5 15-a.  $\text{Ac}_2\text{O}$ ,  $\text{NaOAc}$ ; 15-b. General Method 34; 15-c. General Method 3; 15-d. (a) TBDPS-Cl, 1,2-DCE, imidazole; (b) 2,2-dimethoxy-propane,  $\text{TsOH}$ , MeCN; 15-e. (a) Benzoylchloride, pyridine, 1,2-DCE, DMAP; (b) MeOH,  $\text{TsOH}$ , MeCN; 15-f. General Method 4; 15-g. General Methods 13 and 20; General Method 33.

**Example 16: Synthesis of Glucosyl N-Glycoside Building Block**

- 5    16-a. General Method 34; 16-b. General Method 3; 16-c. General Method 4;  
       16-d. General Method 5; 16-e. General Method 18; 16-f. General Method 19.

Example 17: Synthesis of Glucosylamino 2-Deoxy-2-Amino library.17-a. Synthesis of 2-Deoxy 2-Amino Glycosyl Amine

- 5 To a solution of starting material (20.51mmol) in MeOH/DMF (4:1, 150 mL) was added hydrazine hydrate (92.2mmol) and the reaction mixture was stirred at room temperature for 1.5h. The solution was diluted with ~400mL chloroform, washed with brine, dried over MgSO<sub>4</sub>, filtered and the solvents evaporated. The crude product **457** was directly used for the next step.

10

17-b. Synthesis of 2-Deoxy 2-NHDTPM protected Glycosyl Amine

Compound **458** was formed from reaction of **457** according to the procedure

described in General Method 30.

17-c. Synthesis of 2-Deoxy 2-NHDTPM protected Glycosyl Amine Alkylated in the 3-Position

- 5 Compounds **459** were formed according to the procedure described in General Method 7.

17-d. Reductive Ring Opening of a 2-Deoxy 2-NHDTPM 3-O-Alkyl Glycosyl Amine

- 10 A solution of a derivative represented by **460** (4.37mmol) in dry DCM (30mL) was cooled to 0°C and 44ml of a 1 molar solution of BH<sub>3</sub> in THF (44mmol) and 0.43mL of a 1 molar solution of dibutylboron triflate in DCM (0.43mmol) were added. The reaction mixture was stirred at 0°C and 0.1 eq. of Bu<sub>2</sub>BOTf repeatedly added at 1h intervals until t.l.c. (toluene/EtOAc 1:1) showed  
15 complete conversion (total of 0.5 eq. Bu<sub>2</sub>BOTf). The reaction was quenched by the addition of 8mL Et<sub>3</sub>N and 15mL MeOH at 0°C. After evaporation of the solvents the residue was taken up in 350mL DCM, the solution washed with half saturated brine, filtered over cotton and the solvents evaporated to yield a residue containing the product that was directly used in the next step.

20

17-e. Re-amino Protection of 3-O-Alkyl Glycosyl Amine

- Compounds **461** were formed according to the procedure described in General Method 30; <sup>1</sup>H-NMR, (CDCl<sub>3</sub>): δ 9.92 (dd, 1H, NH, J<sub>NH,2</sub>=9.7 Hz, J<sub>NH,=CH</sub>=13.8 Hz), 7.88 (d, 1H, =CH), 7.75-7.68 (m, 4H, Ar), 7.35-7.22 (m,  
25 5H, Ar), 6.95-6.86 (m, 2H, Ar), 5.08 (d, 1H, NapCH<sub>2</sub>, J<sub>gem</sub>=12.1 Hz), 4.86 (d, 1H, PMPCH<sub>2</sub>, J<sub>gem</sub>=10.5 Hz), 4.72 (d, 1H, PMPCH<sub>2</sub>), 4.71(d, 1H, H-1b, J<sub>1,2</sub>=9.2 Hz), 4.69 (d, 1H, NapCH<sub>2</sub>), 3.95 (dd, 1H, H-6a, J<sub>gem</sub>=12.2 Hz, J<sub>5,6a</sub>=1.7 Hz), 3.85-76 (m, 1H, H-6b), 3.81 (s, 3H, OMe), 3.74 (dd, 1H, H-4, J<sub>3,4</sub>=8.9 Hz, J<sub>4,5</sub>=9.4 Hz), 3.64 (dd, 1H, H-3, J<sub>2,3</sub>=9.3 Hz), 3.49 (ddd, 1H, H-5),  
30 3.22 (s, 3H, NMe), 3.11 (dd, 1H, H-2), 3.05 (s, 3H, NMe).

17-f. Methylation of the 6-Position of a Glycosylamine

Compounds **462** were formed according to the procedure described in

General Method 7;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ );  $\delta$  9.92 (dd, 1H, NH,  $J_{\text{NH}_2}=9.7$  Hz,  $J_{\text{NH}=\text{CH}}=13.8$  Hz), 7.88 (d, 1H,  $=\text{CH}$ ), 7.75-7.68 (m, 4H, Ar), 7.35-7.22 (m, 5H, Ar), 6.95-6.86 (m, 2H, Ar), 5.08 (d, 1H, NapCH<sub>2</sub>,  $J_{\text{gem}}=12.1$  Hz), 4.86 (d, 1H, PMPCH<sub>2</sub>,  $J_{\text{gem}}=10.5$  Hz), 4.72-4.68 (m, 3H, NapCH<sub>2</sub>, PMPCH<sub>2</sub>, H-1), 3.80-3.74 (m, 3H, H-6a, H-6b, H-4), 3.81 (s, 3H, OMe), 3.64 (dd, 1H, H-3,  $J_{2,3}=9.3$  Hz), 3.49 (ddd, 1H, H-5), 3.22 (s, 3H, NMe), 3.11 (dd, 1H, H-2), 3.05 (s, 3H, NMe).

10 17-g. Removal of the DTPM Group of 2-Deoxy-2-Amino Glycosylamine compound

Compounds **463** were formed according to the procedure described in General Method 8;  $^1\text{H-NMR}$ , ( $\text{CDCl}_3$ )  $\delta$  7.78-7.66 (m, 4H, Ar), 7.43-7.32 (m, 5H, Ar), 6.86-6.69 (m, 2H, Ar), 5.48 (s, 1H, CH-PMP), 5.05 (d, 1H, NapCH<sub>2</sub>,  $J_{\text{gem}}=11.3$  Hz), 4.77 (d, 1H, NapCH<sub>2</sub>), 4.47 (d, 1H, H-1b,  $J_{1,2}=8.9$  Hz), 4.28 (dd, 1H, H-6a,  $J_{\text{gem}}=10.3$  Hz,  $J_{5,6a}=5.5$  Hz), 3.76-3.65 (m, 2H, H-6b, H-4), 3.72 (s, 3H, OMe), 3.49 (dd, 1H, H-3,  $J_{2,3}=9.0$  Hz,  $J_{3,4}=9.0$  Hz), 3.46 (ddd, 1H, H-5), 2.75 (dd, 1H, H-2).

20 17-h. Synthesis of a 2-Deoxy-2-N-Acyl Glycosyl Amine

The compounds **464** were synthesised according to the procedure described in General Method 31.

17-i. Solution Phase Reduction of an Anomeric Azide

25 The compounds **465** were synthesised according to the procedure described in General Method 13.

17-j. Formation of 1-N-Acyl Derivatives of a Glucosaminyll Derivative.

The compounds **466** synthesised according to the procedure described in General Method 31.

30

17-k. Removal of a Boc Protecting Group from a 2-Deoxy-2-N-Acyl-Glycosylamine Derivative.

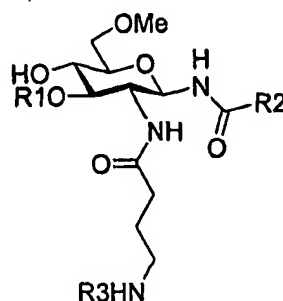
Dissolve crude **467** (~0.21mmol) in 10mL 20% TFA in DCM and stir at room

temperature for 10min. Evaporate solvents and dry the remaining syrup under high vacuum. Redissolve in DCM and wash with 1M KOH, filter over cotton, evaporate and purify by column chromatography (eluent DCM/MeOH 10:1 1% Et<sub>3</sub>N) to give the product (for the formation of compounds **469**, **470**, **471**).

5 Yield typically 35% over two steps.

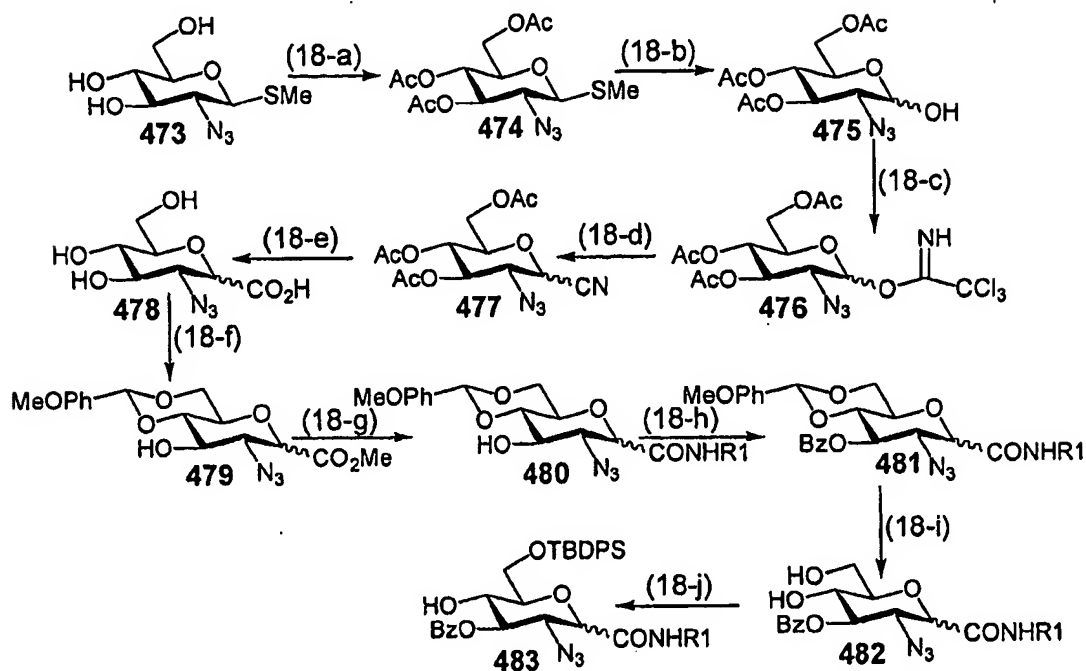
17-I. Solution Phase Guanylation (only for the formation of compound **472**)

To a solution of crude **467** (max. 0.22mmol) in dry DMF were added 89mg (0.44mmol) 3,5-dimethylpyrazole-1-carboxamidine nitrate and 84  $\mu$ L (0.48mmol) DIPEA and the reaction mixture stirred for 3h. The solvents were evaporated and the residue dried under high vacuum to give 280mg of a mixture containing the desired product. The purification using preparative HPLC gave 8mg of the pure product **472**.

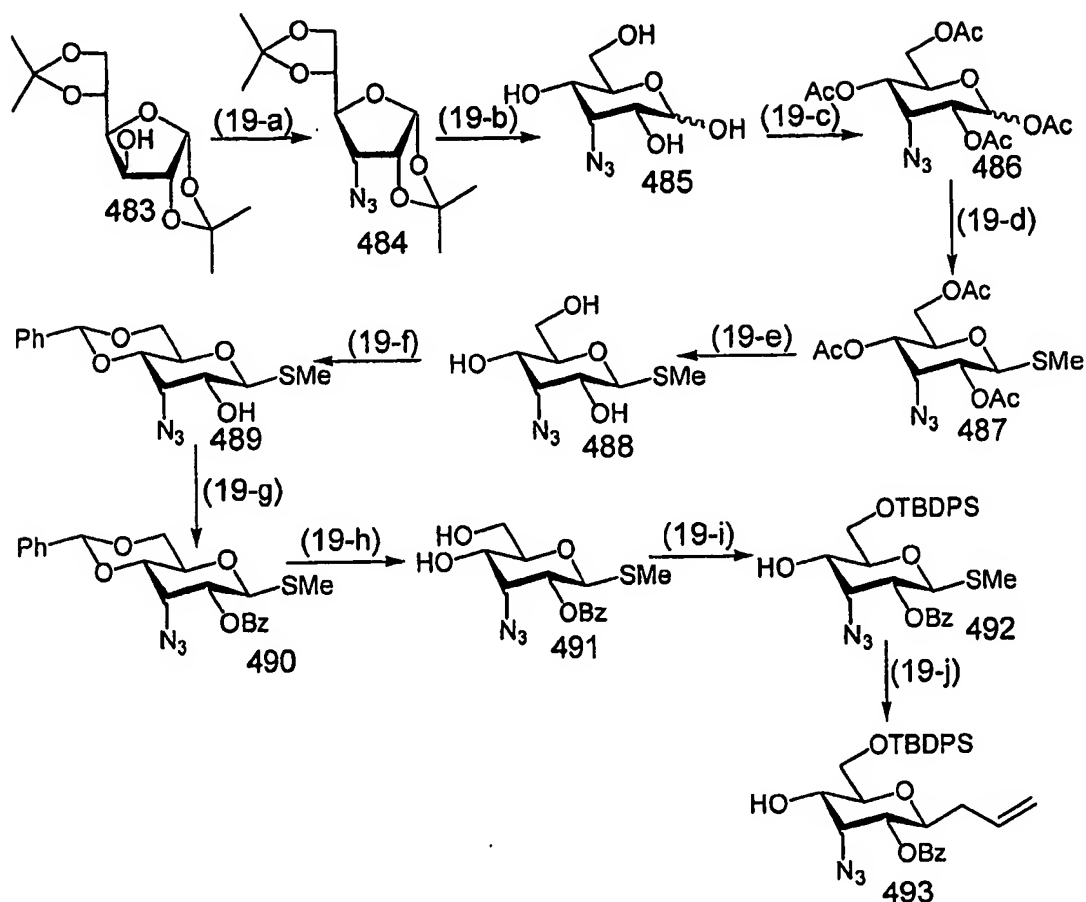


15

| Comp.      | R1             | R2                 | R3                   | Molecular Ion               |
|------------|----------------|--------------------|----------------------|-----------------------------|
| <b>469</b> | naphthyl       | phenyl             | H                    | [M+H] <sup>+</sup> = 522.33 |
| <b>470</b> | naphthyl       | 4-Chlorophenyl     | H                    | [M+H] <sup>+</sup> = 556.1  |
| <b>471</b> | naphthyl       | benzyl             | H                    | [M+H] <sup>+</sup> = 536.36 |
| <b>472</b> | 4-chlorobenzyl | $\alpha$ -naphthyl | C(NH)NH <sub>2</sub> | [M+H] <sup>+</sup> = 598.39 |

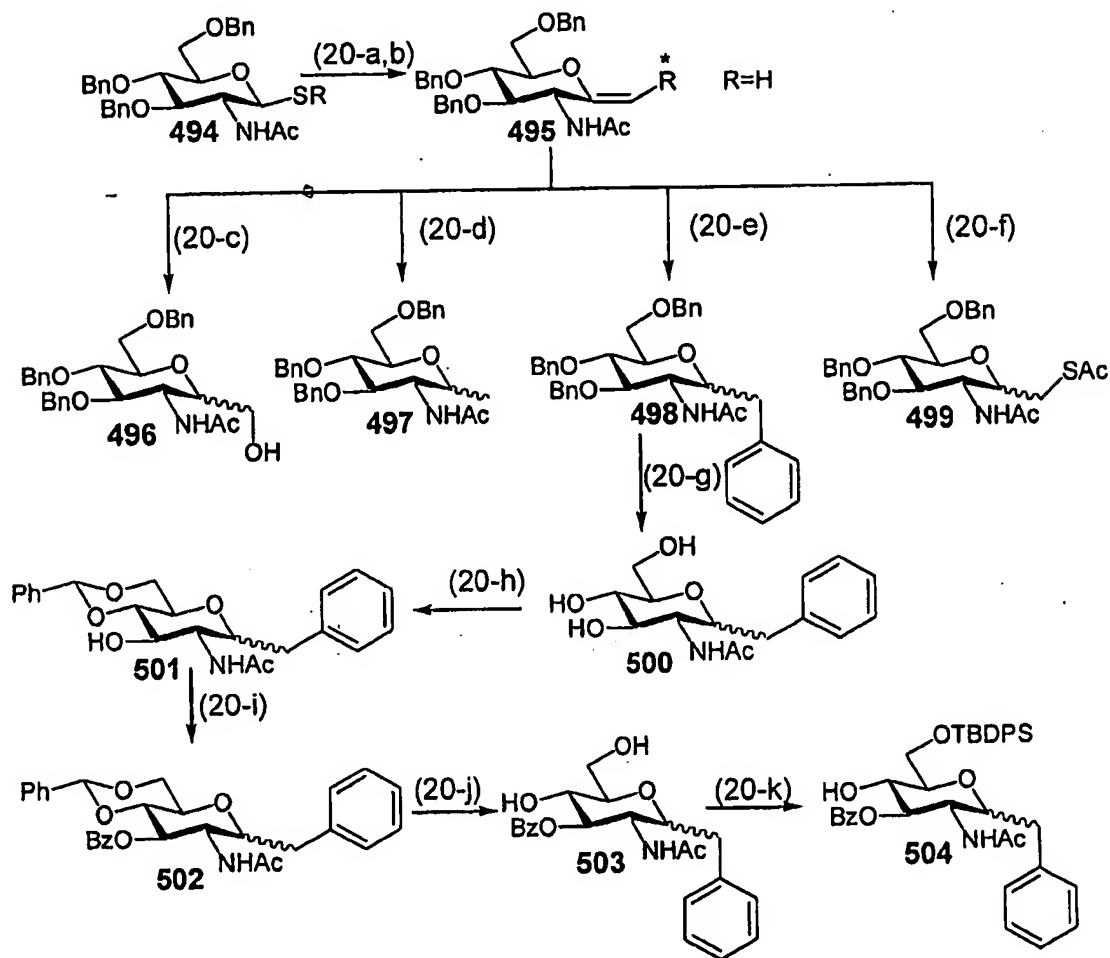
Example 18: Synthesis of a Carboxamide C-Glycoside 1

- 5 **Conditions:** NaOMe/MeOH; (ii) Acetone, NBS; (iii) trichloroacetone, potassium carbonate, DCM; (iv) TMS-CN, TMS-Of, DCM; (v) NaOH/H<sub>2</sub>O<sub>2</sub>; (vi) (a) TMS-CH<sub>2</sub>N<sub>2</sub>; (b) *p*-methoxybenzaldehyde dimethylacetal, CSA, MeCN, DMF; (vii) (a) LiOH, H<sub>2</sub>O, THF; (b) HBTU, DIPEA, DMF, R<sup>1</sup>-NH<sub>2</sub>; (viii) benzoylchloride, pyridine, 1,2-DCE, DMAP; (TsOH, MeOH, MeCN, H<sub>2</sub>O; (x)
- 10 TBBDPS-Cl, imidazole, 1,2-DCE.

Example 19: Synthesis of an Allyl C-Glycoside

- 5 **Conditions:** (i)  $\text{TiF}_2\text{O}$ , pyridine, DCM; (b)  $\text{NaN}_3$ , DMF; (ii) acetone,  $\text{H}^+$ ; (iii)  $\text{Ac}_2\text{O}$ , pyridine; (iv) hexamethyldisilazane,  $\text{I}_2$ ,  $\text{CH}_3\text{-S-S-CH}_3$ ; (v)  $\text{NaOMe/MeOH}$ ; (vi)  $\text{TsOH}$ ,  $\alpha,\alpha$ -dimethoxytoluene, MeCN; (vii) benzoylchloride, 1,2-DCE, pyridine, DMAP; (viii)  $\text{TsOH}$ , MeOH,  $\text{H}_2\text{O}$ , MeCN; (ix) TBDPS-Cl, imidazole, 1,2-DCE; (x) TMS-allyl, TMS-OTf, DCM.

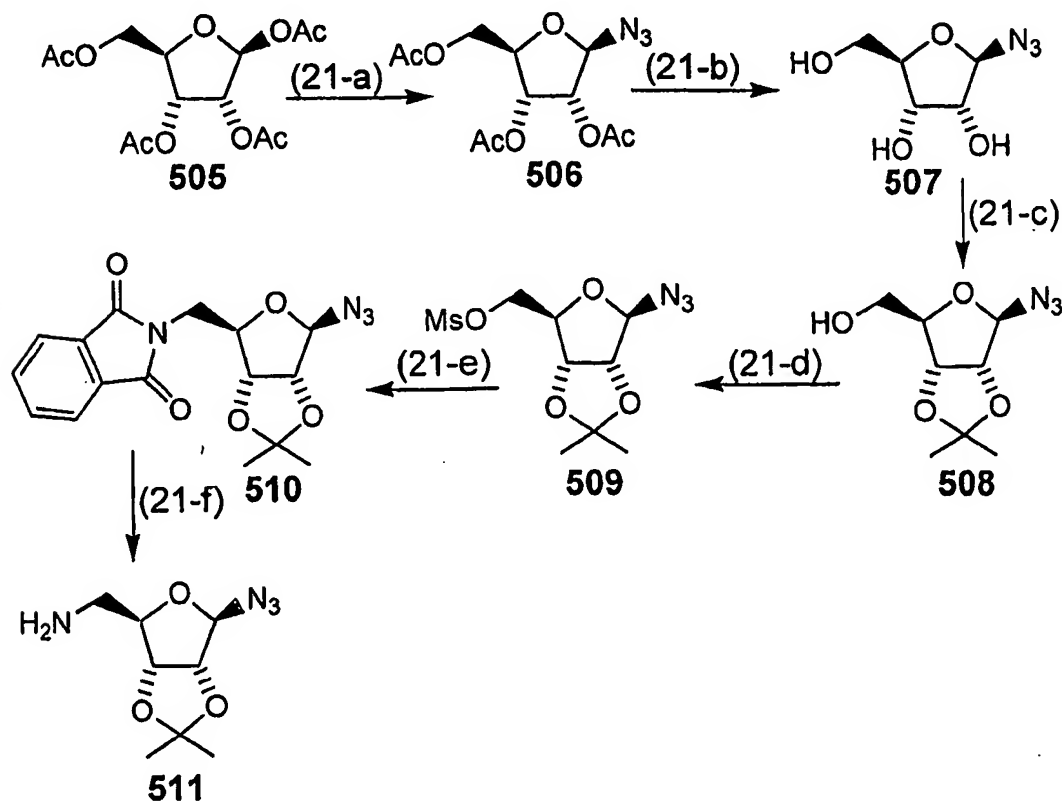


Example 20: Synthesis of a Range of C-Glycosides

5

\*Ramburg-Backlund rearrangement of phthalimido thioglycosides I to give an exo methylene compound II. The products can then be converted to a variety of C-glycosides which can be further elaborated to building blocks as exemplified by 28. The reaction pathway can furnish C-glycosides with a large

10 number of alkyl or aromatic side-chains at the anomeric position. *Conditions:* (i) Oxone, (ii) KOH, CCl<sub>4</sub>, (iii) BH<sub>3</sub>, HOOH, H<sub>2</sub>/Pd; (iv) H<sub>2</sub>/Pd; (v) ArX, Pd(0), H<sub>2</sub>/Pd; (vi) AcSH, AIBN, H<sub>2</sub>/Pd; (vii) (a) KOH, (b) TfN<sub>3</sub>, RT, CH<sub>2</sub>Cl<sub>2</sub>, MeOH, H<sub>2</sub>O/cat. CuSO<sub>4</sub>, 90%; (viii) α,α-dimethoxytoluene, TsOH, MeCN/MeOH; (ix) BzCl, pyridine, (x) MeOH/MeCN/H<sub>2</sub>O, TsOH; (xi) TBDPS-Cl, pyridine.

Example 21: Synthesis of an Ribofuranosyl Azide Building Block.**21-a. 1-Azido-2,3,5-triacetyl ribose **506****

To a solution of 1,2,3,5-tetraacetyl ribose **505** (0.189 mol) in dry DCM (480 ml) at room temperature was added trimethylsilyl azide (0.211 mol) followed by a solution of anhydrous  $\text{SnCl}_4$  (9.40 mmol) in dry DCM (60 ml). The resulting colourless solution was stirred at room temperature overnight. The solution was washed with saturated sodium bicarbonate. The combined organic extracts were dried ( $\text{MgSO}_4$ ) and the solvent was removed in vacuo to give a colourless oil, 100 %.

**21-b. 1-Azido ribose **507****

The compound was synthesised according to the procedure described in General Method 1 (used directly in the following step).

**21-c. 1-Azido-2,3-isopropylidene ribose **508****

A solution of 1-azido ribose **507** (0.2 mol) in dry acetone (120 ml) and 2,2-

dimethoxypropane (488 mmol) at room temperature and under nitrogen was treated with conc. sulfuric acid (16.9 mmol). The resulting solution was stirred at room temperature for 30 min. The reaction was quenched with pyridine and the solvent was removed in vacuo. The residue was dissolved in DCM (500 ml), washed with 10 % citric acid and saturated sodium bicarbonate, dried (MgSO<sub>4</sub>) and the solvent was removed in vacuo to give a yellow oil which was purified by a squat column on silica gel (20-40 % EtOAc/petrol) to give a yellow oil **508**, 69 % from tetraacetate **505**.  $\delta_H$  (400 MHz: CDCl<sub>3</sub>) 1.32 (s, 3H, CH<sub>3</sub>), 1.50 (s, 3H, CH<sub>3</sub>), 2.31 (dd, *J* 8.0, 5.2 Hz, 1H, OH), 3.67 (ddd, *J* 12.4, 7.6, 4.8 Hz, 1H, H5a), 3.77 (ddd, *J* 12.4, 6.2, 4.0 Hz, 1H, H5b), 4.41 (dd, *J* 5.2, 4.8 Hz, 1H, H4), 4.52 (d, *J* 6.0 Hz, 1H, H3), 4.77 (d, *J* 6.0 Hz, 1H, H2), 5.54 (s, 1H, H1).

21-d. 1-Azido-2,3-isopropylidene-5'-mesylate ribose **509**

Methanesulfonyl chloride (18.1 mmol) was added over one min. to a suspension of the 2,3-isopropylidene ribose **508** (16.5 mmol) in dry pyridine (11 ml) at 0 °C and under N<sub>2</sub>. The resulting suspension was stirred at 0 °C for 2.5 h, then quenched with water (20 ml) and extracted with ethyl acetate (2 x 20 ml). The combined organic extracts were washed with 10 % citric acid and saturated NaHCO<sub>3</sub>, dried (MgSO<sub>4</sub>), and the solvent was removed in vacuo to give a pale yellow oil which was purified by a squat column on silica gel (20-40 % EtOAc/petrol) to give a white solid, 88 %. LCMS: >90 % by ELSD, (M – N<sub>3</sub>)<sup>+</sup> 251.  $\delta_H$  (400 MHz: CDCl<sub>3</sub>) 1.31 (s, 3H, CH<sub>3</sub>), 1.49 (s, 3H, CH<sub>3</sub>), 3.09 (s, 3H, SO<sub>2</sub>CH<sub>3</sub>), 4.28 (dd, *J* 10.6, 6.8 Hz, 1H, H5a), 4.30 (dd, *J* 10.6, 6.0 Hz, 1H, H5b), 4.50 (td, *J* 6.1, 1.2 Hz, 2H, H3, H4), 4.72 (dd, *J* 6.0, 1.3 Hz, 1H, H2), 5.56 (s, 1H, H1).

21-e. 1-Azido-2,3-isopropylidene-5'-phthalimido-ribose **510**

A suspension of sugar derivative **509** (14.3 mmol), potassium phthalimide (18.8 mmol) and sodium iodide (2.86 mmol) in DMF (105 ml) was heated at 100 °C for 30 min., then cooled to room temperature and diluted with water (500 ml) and cooled in an ice-water bath. The resulting product were collected by vacuum filtration, washed with water and dried over P<sub>2</sub>O<sub>5</sub> in a dessicator

overnight as white crystals, 51 %. LCMS: >95 % by ELSD,  $(2M + H)^+$  711.  $\delta_H$  (400 MHz:  $CDCl_3$ ) 1.29 (s, 3H,  $CH_3$ ), 1.45 (s, 3H,  $CH_3$ ), 3.91 (dd,  $J$  13.9, 8.4 Hz, 1H,  $H5_a$ ), 3.95 (dd,  $J$  13.9, 6.5 Hz, 1H,  $H5_b$ ), 4.57 (t,  $J$  6.4 Hz, 2H,  $H3$ ,  $H4$ ), 4.78 (d,  $J$  5.8 Hz, 1H,  $H2$ ), 5.57 (s, 1H,  $H1$ ), 7.73 (d,  $J$  3.2 Hz, 1H, ArH),  
5 7.74 (d,  $J$  3.2 Hz, 1H, ArH), 7.87 (d,  $J$  3.2 Hz, 1H, ArH), 7.88 (d,  $J$  3.2 Hz, 1H, ArH).

**21-f. 1-Azido-2,3-isopropylidene-5'-amino-ribose 511**

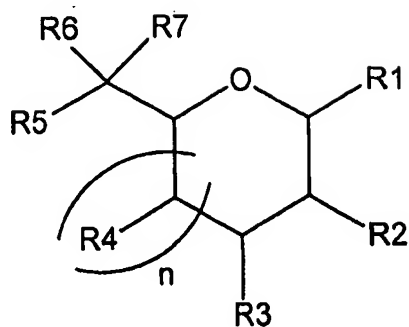
A suspension of sugar derivative **510** (8.13 mmol) in methanol (21 ml) was  
10 treated with hydrazine hydrate (12.0 mmol) to give a pale yellow solution which was heated at reflux for 2 h. The methanol was removed in vacuo from the resulting suspension and the residue was dissolved in water (40 ml) and acidified (to pH 1) with conc. HCl. The resulting precipitate was removed by vacuum filtration and washed with water. To the filtrate was added solid  
15 sodium hydroxide (to pH 10) and the product was extracted with  $CHCl_3$  and dried ( $MgSO_4$ ). The solvent was removed in vacuo to give a yellow oil, 93 %. LCMS:  $(M - N_3)^+ = 172$ ;  $\delta$  (400 MHz:  $CDCl_3$ ) 1.32 (bs, 5H,  $CH_3$ ,  $NH_2$ ), 1.50 (s, 3H,  $CH_3$ ), 2.84 (dd,  $J$  13.1, 6.0 Hz, 1H,  $H5_a$ ), 2.90 (dd,  $J$  13.0, 8.1 Hz, 1H,  $H5_b$ ), 4.24 (t,  $J$  7.0 Hz, 1H,  $H4$ ), 4.48 (d,  $J$  5.8 Hz, 1H,  $H3$ ), 4.61 (d,  $J$  4.8 Hz,  
20 1H,  $H2$ ), 5.53 (s, 1H,  $H1$ ).

References

1. K. C. Nicolaou; J. M. Salvino, K. Raynor; S. Pietranico; T. Reisine; R. M. Freidinger, R. Hirschmann, *Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp.*, 11<sup>th</sup>, 1990
- 5 2. (a) H. Kunz, T. Wundberg, C. Kallus, T. Opatz, S. Henke, W. Schmidt, *Angew. Chem. Int. Ed.*, 1998, 37, No. 18, (b) K. Kallus, T. Wundberg, W. Schmidt, S. Henke, H. Kunz, *Tet. Lett.*, 40, 1999, 7783-7786, (c) U. Hüniger, T. Maidhof, O. Knöll, H. Kunz, *Poster Presentation*, 20<sup>th</sup> International Carbohydrate Symposium, Hamburg-Germany, (d) T. Opatz,  
10 C. Kallus, T. Wundberg, W. Schmidt, S. Henke, H. Kunz, *Poster Presentation*, 20<sup>th</sup> International Carbohydrate Symposium, Hamburg-Germany.
- 15 3. R. Hirschmann, K.C. Nicolaou, S. Pietramico, J. Salvino, E.M. Lealy, W.C. Shakepeare, P.S. Spengler, P. Hamley, A.B. Smith, T. Reisine, K. Raynor, C. Donaldson, W. Vale, L. Maechler, R.M. Freidinger, C.D. Strader, *J. Am. Chem. Soc.*, 1993, 115, 12550

Claims:

1. A compound of formula I



formula I

5

Wherein,

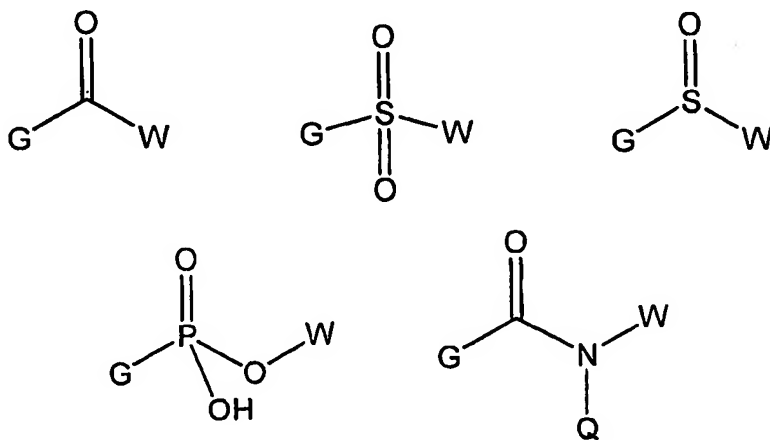
n is 0 or 1;

R6 and R7 are hydrogen, or together form a carbonyl oxygen;

10 R1 is selected from the group consisting of hydrogen; -N(Z)Y and -C(Z)Y wherein;

When R1 is -N(Z)Y, then:

15 Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(Y)Z;



Z is selected from hydrogen or X1;

Q is selected from hydrogen or W;

The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

5

The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

10 When R1 is  $-C(Z)Y$ , then:

Y is selected from the group consisting of two hydrogen atoms, a double bonded oxygen ( $=O$ ) to form a carbonyl, and a triple bonded nitrogen to form a nitrile,

15

Z is absent, or is selected from hydrogen or U,

Wherein U is selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aminoalkyl, aminoaryl, aryloxy, alkoxy, heteroaryloxy, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

20

When R1 is H, at least two of the groups R2, R3, R4 and R5 are selected from the group consisting of  $-OX_2$  or  $-N(T)Y$ , and the others are independently selected from hydrogen,  $-OH$ ,  $-OX_2$ ,  $-N(T)Y$ , wherein Y is as defined above, T is selected from hydrogen or  $X_2$ ; and  $X_2$  is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,

25

When R1 is  $N(Z)Y$  or  $C(Z)Y$ , at least one of the groups R2, R3, R4 and R5 are selected from the group consisting of  $-OX_2$  or  $-N(T)Y$ , and the others are independently selected from hydrogen,  $-OH$ ,  $-OX_2$ ,  $-N(T)Y$ , wherein Y is as defined above, T is selected from hydrogen or  $X_2$ ; and  $X_2$  is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,

30

2. The compound of claim 1, wherein wherein the ring is selected from the pyran or furan form and the anomeric center is selected from the  $\alpha$  or  $\beta$  configuration.

5

3. The compound of claim 1, wherein the groups Z and Y are combined to form a monocyclic or bicyclic ring structure of 4 to 10 atoms.

4. The compound of claim 3, wherein the ring structure is further  
10 substituted with X1 groups.

5. The compound of claim 1 in wherein W is substituted with a moiety selected from the group consisting of OH, NO, NO<sub>2</sub>, NH<sub>2</sub>, N<sub>3</sub>, halogen, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid,  
15 carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate, phosphoramidate, hydrazide, hydroxamate, hydroxamic acid.

20 6. The compound of claim 1 in wherein X1 is substituted with a moiety selected from the group consisting of OH, NO, NO<sub>2</sub>, NH<sub>2</sub>, N<sub>3</sub>, halogen, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl,  
25 substituted or unsubstituted imine, sulfate, sulfonamide, phosphate, phosphoramidate, hydrazide, hydroxamate and hydroxamic acid.

7. The compound of claim 1 in wherein U is substituted with a moiety selected from the group consisting of OH, NO, NO<sub>2</sub>, NH<sub>2</sub>, N<sub>3</sub>, halogen, CF<sub>3</sub>,  
30 CHF<sub>2</sub>, CH<sub>2</sub>F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate,

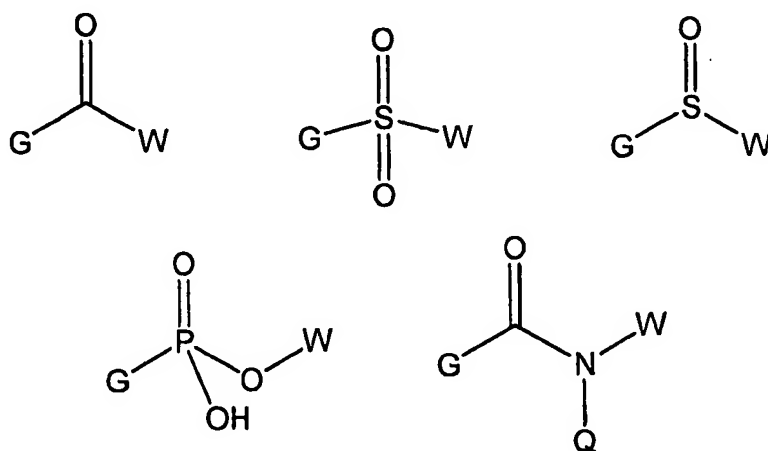


phosphoramidate, hydrazide, hydroxamate, hydroxamic acid, heteroaryloxy, aminoalkyl, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl and thioheteroaryl.

8. The compound of claim 1 wherein X2 is substituted with a moiety  
5 selected from the group consisting of OH, NO, NO<sub>2</sub>, NH<sub>2</sub>, N<sub>3</sub>, halogen, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate,  
10 phosphoramidate, hydrazide, hydroxamate and hydroxamic acid.
9. The compound of claim 1 wherein at least three of the groups R2, R3, R4 and R5 are selected from -OX2 or -N(T)Y;
- 15 10. The compound of claim 1 wherein R1 is hydrogen.
11. The compound of claim 10 wherein independently at least one of R2, R3, R4, or R6 is -N(T)Y, and at least one is -OX2.
- 20 12. The compound of claim 10 wherein independently at least two of R2, R3, R4, or R6 are -OX2.
13. The compound of claim 10 wherein at least two of R2, R3, R4, or R6 is -N(T)Y.
- 25 14. The compound of claim 1 wherein R1 is -N(Z)Y.
15. The compound of claim 14 wherein at least one of R2, R3, R4, or R6 is -N(T)Y.
- 30 16. The compound of claim 14 wherein at least two of R2, R3, R4, or R6 is -N(T)Y.

17. The compound of claim 14 wherein at least two of R2, R3, R4, or R6 are -OX2.

18. A method of synthesis of compounds of claim 10, wherein n is 1,  
 5 comprising the step of reducing a synthetic intermediate of formula III,  
 in which  
 V is bromine or chlorine,  
 R6 and R7 are hydrogen, or together form a carbonyl oxygen,  
 R5, R4, R3, and R2 are selected from the group consisting of OH, O-acyl, N3,  
 10 NHDde, NHDTPM, NHZ, NHBOC, phthalimide, OX2, N(T)Y and an O-  
 protecting group,  
 X2 is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl,  
 heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,  
 T is hydrogen or X2,  
 15 Y is selected from hydrogen, or the following, where G denotes the point of  
 connection to the nitrogen atom in N(T)Y;



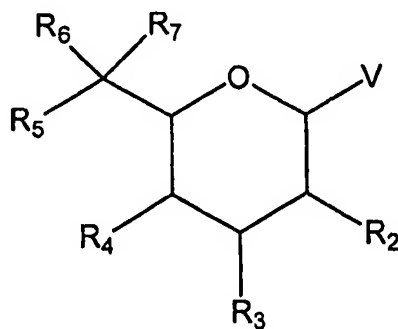
20 Z is selected from hydrogen or X1;

Q is selected from hydrogen or W;

The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

25

The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,



general formula III

5

19. The method of claim 18, wherein R6 and R7 together form a carbonyl oxygen and R5 is O-alkyl, O-arylalkyl or O-aryl.

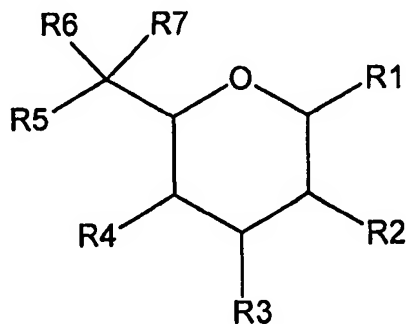
10 20. The method of claim 19, wherein the R5 substituent is substituted with a moiety selected from the group consisting of OH, NO, NO<sub>2</sub>, NH<sub>2</sub>, N<sub>3</sub>, halogen, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl,  
15 carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate, phosphoramidate, hydrazide, hydroxamate, hydroxamic acid.

21. The method of claim 18, wherein the O- protecting groups comprise acetals and ketals which protect two adjacent oxygens.

20

22. A method of synthesis of compounds according to claim 14, in which n is 1, comprising the step of reacting a compound of formula III with an azide nucleophile, to form an anomeric azide and reduction of the anomeric azide to form an anomeric amine and reaction of the anomeric amine with an  
25 electrophile.

23. A method of combinatorial synthesis of compounds of claim 1, wherein n is 1, comprising the step of immobilizing a compound of formula IV onto a support.



general formula IV

5

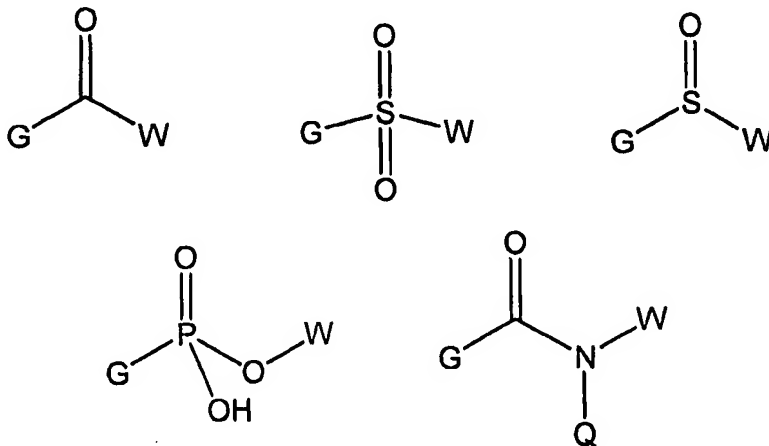
wherein

R6 and R7 are hydrogen, or together form a carbonyl oxygen;

R1 is selected from the group consisting of hydrogen; -N(Z)Y and -C(Z)Y wherein;

10 When R1 is -N(Z)Y, then:

Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(Y)Z;



15

Z is selected from hydrogen or X1;

Q is selected from hydrogen or W;

The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

- 5           The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

When R1 is  $-C(Z)Y$ , then:

10

Y is selected from the group consisting of two hydrogen atoms, a double bonded oxygen ( $=O$ ) to form a carbonyl, and a triple bonded nitrogen to form a nitrile,

Z is absent, or is selected from hydrogen or U,

15

Wherein U is selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aminoalkyl, aminoaryl, aryloxy, alkoxy, heteroaryloxy, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

20

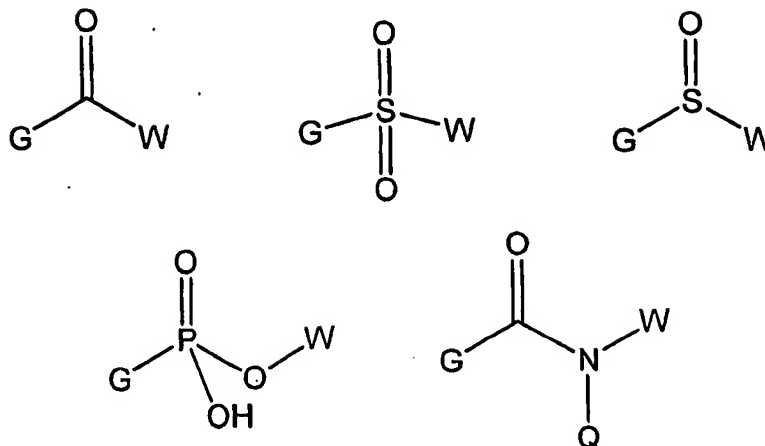
R5, R4, R3, and R2 are selected from the group consisting of OH, O-acyl,  $N_3$ , NHDde, NHDTPM, NHZ, NHBOC, phthalimide, OX2,  $N(T)Y$  and an O-protecting group, and the linkage between the compound of formula IV and the support is through any one of positions R1, R2, R3, R4 or R5,

X2 is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,

25

T is hydrogen or X2,

Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in  $N(Y)Z$ ;



Z is selected from hydrogen or X1;

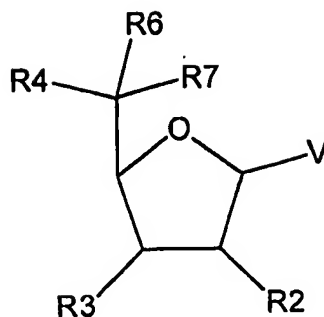
Q is selected from hydrogen or W;

- 5        The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

- 10       The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

24.     The method of claim 23 wherein the support is selected from the group consisting of derivatised polystyrene, tentagel, wang resin, MBHA  
15     resin, aminomethylpolystyrene, rink amide resin DOX-mpeg, and polyethylene glycol.

25.     A method of synthesis of compounds according to claim 13, in which  
20     n is 0, comprising the step of reacting a compound of formula V in the presence of a lewis acid with an azide source to form an anomeric azide, reduction of the anomeric azide to form an anomeric amine and reaction of the anomeric amine with an electrophile.



general formula V

in which V is -OAcyl,

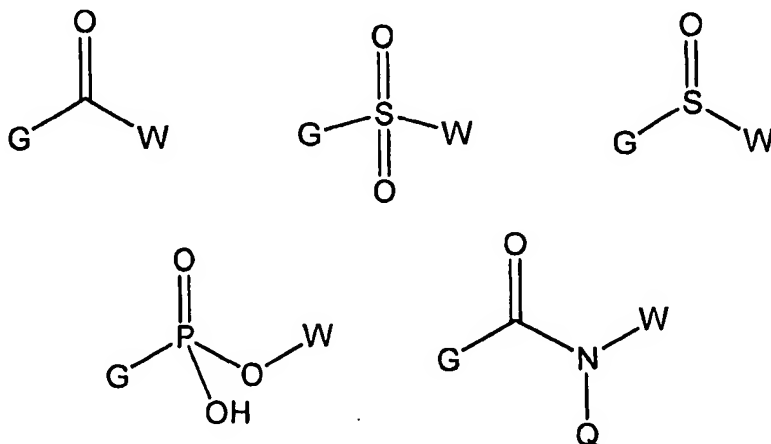
R6 and R7 are hydrogen, or together form a carbonyl oxygen,

- 5 R4, R3, and R2 are selected from the group consisting of OH, O-acyl, N<sub>3</sub>, NHDde, NHDTPM, NHZ, NHBOC, phthalimide, OX2, N(T)Y and O-protecting group,

X2 is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,

- 10 T is hydrogen or X2,

Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(Y)Z;



- 15

Z is selected from hydrogen or X1;

Q is selected from hydrogen or W;

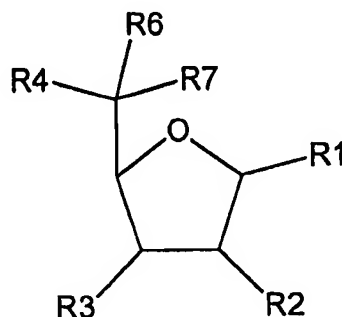
The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

26. The method of claim 25, wherein R6 and R7 together form a carbonyl oxygen, and R4 is substituted O-alkyl, O-arylalkyl or O-aryl.

10

27. A method of combinatorial synthesis of compounds of claim 1, wherein n is 0, comprising the step of immobilizing a compound of formula VI onto a support,



general formula VI

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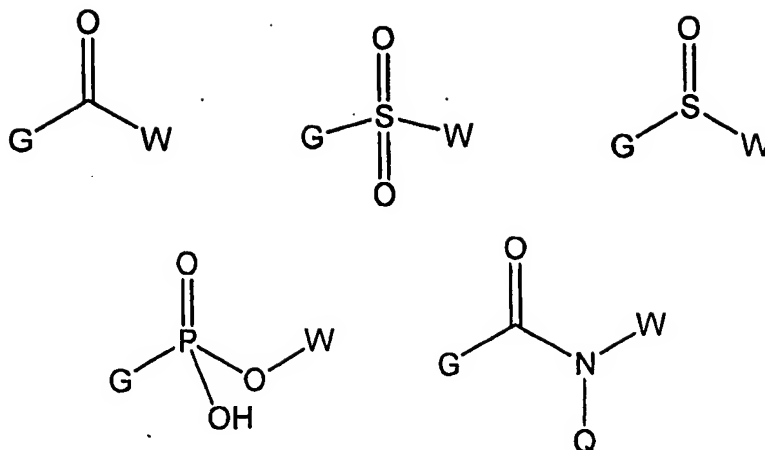
Wherein R1 is selected from the group consisting of hydrogen; -N(Z)Y and -C(Z)Y wherein;

When R1 is -N(Z)Y, then:

Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(Y)Z;

20





Z is selected from hydrogen or X1;

Q is selected from hydrogen or W;

- 5 The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

- 10 The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

When R1 is  $-C(Z)Y$ , then:

- 15 Y is selected from the group consisting of two hydrogen atoms, a double bonded oxygen ( $=O$ ) to form a carbonyl, and a triple bonded nitrogen to form a nitrile,

Z is absent, or is selected from hydrogen or U,

- 20 Wherein U is selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aminoalkyl, aminoaryl, aryloxy, alkoxy, heteroaryloxy, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

R6 and R7 are hydrogen, or together form a carbonyl oxygen,

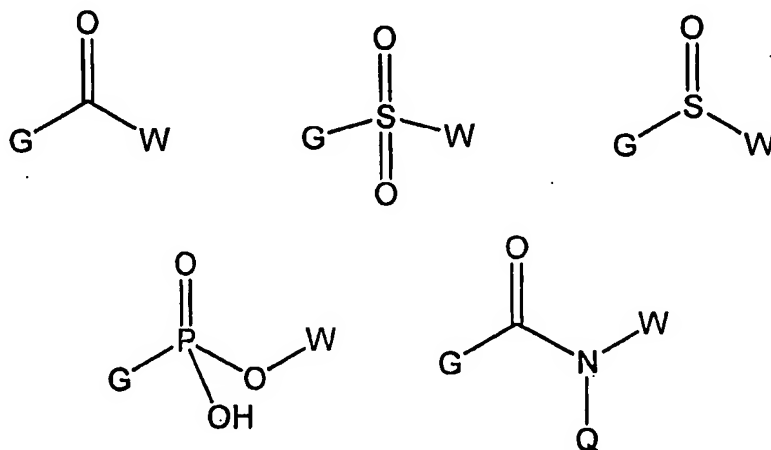
- 25 R4, R3, and R2 are selected from the group consisting of OH, O-acyl,  $N_3$ ,

NHDde, NHDTPM, NHZ, NHBOC, phthalimide, OX<sub>2</sub>, N(T)Y and O-protecting group,

X<sub>2</sub> is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,

5 T is hydrogen or X<sub>2</sub>,

Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(Y)Z;



10

Z is selected from hydrogen or X<sub>1</sub>;

Q is selected from hydrogen or W;

The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and

15 heteroarylalkyl of 1 to 20 atoms ,

The groups X<sub>1</sub> are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

and the linkage between the compound of formula VI and the support is

20 through any one of positions R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, or R<sub>4</sub>.

28. The method of claim 27, wherein the support is selected from the group consisting of derivatised polystyrene, tentagel, wang resin, MBHA resin, aminomethylpolystyrene, rink amide resin DOX-mpeg, and polyethylene glycol.

25

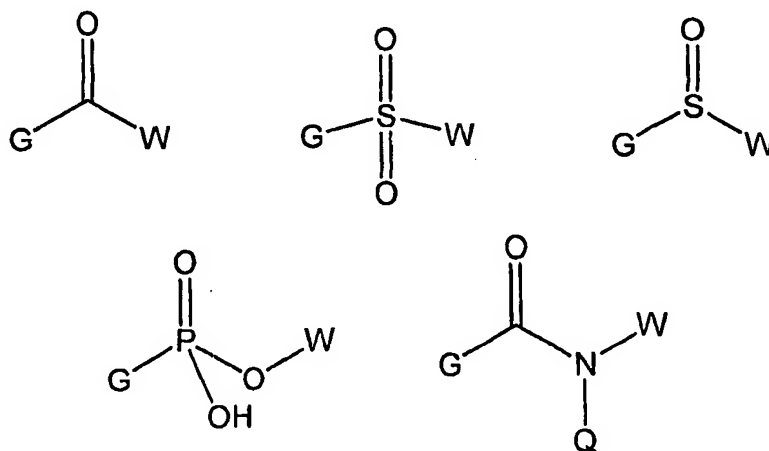
29. A method of solution phase combinatorial synthesis of compounds of claim 1, comprising the step of alkylating a free hydroxyl on a compound of formula IV or formula VI, wherein

5 R6 and R7 are hydrogen, or together form a carbonyl oxygen;

R1 is selected from the group consisting of hydrogen; -N(Z)Y and -C(Z)Y wherein;

When R1 is -N(Z)Y, then:

10 Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(Y)Z;



Z is selected from hydrogen or X1;

15 Q is selected from hydrogen or W;

The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

20 The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

When R1 is -C(Z)Y, then:

25

Y is selected from the group consisting of two hydrogen atoms, a double bonded oxygen (=O) to form a carbonyl, and a triple bonded nitrogen to form a nitrile,

Z is absent, or is selected from hydrogen or U,

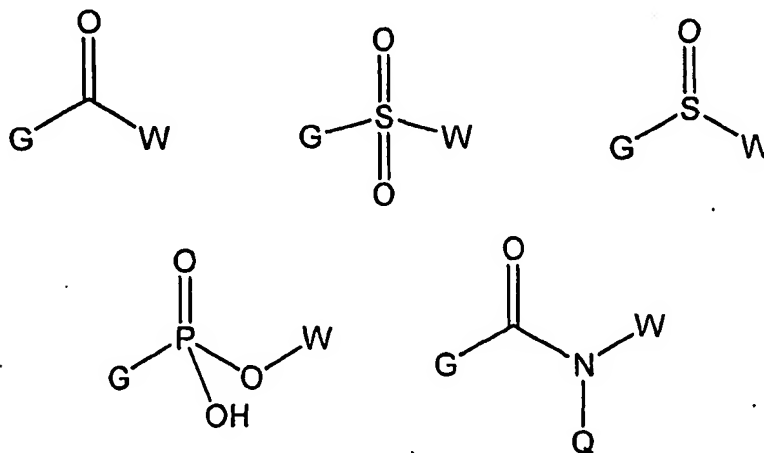
- 5       Wherein U is selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aminoalkyl, aminoaryl, aryloxy, alkoxy, heteroaryloxy, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

- 10   R5, R4, R3, and R2 are selected from the group consisting of OH, O-acyl, N<sub>3</sub>, NHDde, NHDTPM, NHZ, NHBOC, phthalimide, OX2, N(T)Y and an O-protecting group,

X2 is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,

- 15   T is hydrogen or X2,

Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(Y)Z;



- 20

Z is selected from hydrogen or X1;

Q is selected from hydrogen or W;

The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and

- 25   heteroarylalkyl of 1 to 20 atoms,

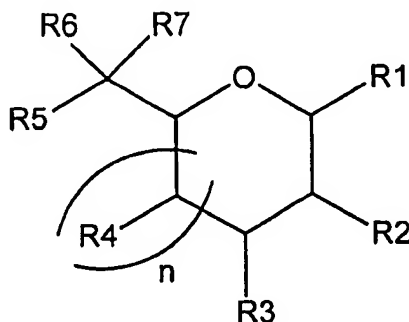
The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

- 5 and any one of the protecting substituents may be removed prior to alkylation.

## AMENDED CLAIMS

[received by the International Bureau on 20 August 2003 (20.08.03) ;  
original claim 1 replaced by new claim 1 ;  
remaining claims unchanged]

1. A compound of formula I



formula I

5

Wherein,

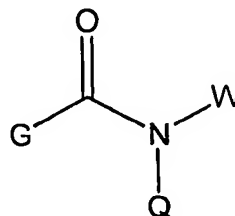
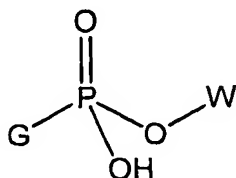
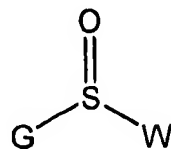
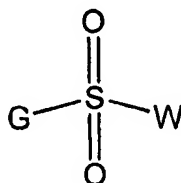
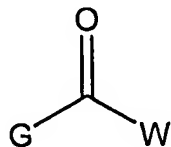
n is 0 or 1;

R6 and R7 are hydrogen, or together form a carbonyl oxygen;

- 10 R1 is selected from the group consisting of hydrogen; -N(Z)Y and -C(Z)Y wherein;

When R1 is -N(Z)Y, then:

- 15 Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(Y)Z;



Z is selected from hydrogen or X1;

Q is selected from hydrogen or W;

The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

5

The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

10 When R1 is  $-C(Z)Y$ , then:

Y is selected from the group consisting of two hydrogen atoms, a double bonded oxygen ( $=O$ ) to form a carbonyl, and a triple bonded nitrogen to form a nitrile,

15 Z is absent, or is selected from hydrogen or U,

Wherein U is selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aminoalkyl, aminoaryl, aryloxy, alkoxy, heteroaryloxy, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

20

When R1 is H, at least two of the groups R2, R3, R4 and R5 are selected from the group consisting of  $-OX_2$  or  $-N(T)Y$ , and the others are independently selected from hydrogen,  $-OH$ ,  $-OX_2$ ,  $-N(T)Y$ , wherein Y is as defined above, T is selected from hydrogen or  $X_2$ ; and  $X_2$  is independently  
25 selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,

When R1 is  $N(Z)Y$  or  $C(Z)Y$ , at least one of the groups R2, R3, R4 and R5 are selected from the group consisting of  $-OX_2$  or  $-N(T)Y$ , and the  
30 others are independently selected from hydrogen,  $-OH$ ,  $-OX_2$ ,  $-N(T)Y$ , wherein Y is as defined above, T is selected from hydrogen or  $X_2$ ; and  $X_2$  is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,

With the provisos that:

- a. the groups R1 to R5 may not combine together to form a cyclic structure,
  - b. X2 may not be another carbohydrate ring, a cyclitol ring or contain another carbohydrate ring,
  - c. all of the X2 substituents may not be the same, and
  - d. when R1 is C(Z)Y, and Z is C=O and R5 is N(T)Y, both T and Y may not be hydrogen, or Y may not be an amino acid or peptide.
2. The compound of claim 1, wherein wherein the ring is selected from the pyran or furan form and the anomeric center is selected from the  $\alpha$  or  $\beta$  configuration.
3. The compound of claim 1, wherein the groups Z and Y are combined to form a monocyclic or bicyclic ring structure of 4 to 10 atoms.
4. The compound of claim 3, wherein the ring structure is further substituted with X1 groups.
5. The compound of claim 1 in wherein W is substituted with a moiety selected from the group consisting of OH, NO, NO<sub>2</sub>, NH<sub>2</sub>, N<sub>3</sub>, halogen, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate, phosphoramidate, hydrazide, hydroxamate, hydroxamic acid.
6. The compound of claim 1 in wherein X1 is substituted with a moiety selected from the group consisting of OH, NO, NO<sub>2</sub>, NH<sub>2</sub>, N<sub>3</sub>, halogen, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate,

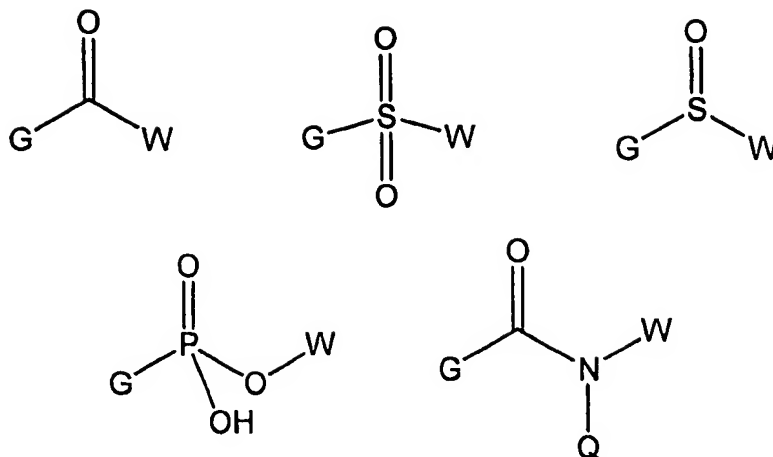


phosphoramidate, hydrazide, hydroxamate and hydroxamic acid.

7. The compound of claim 1 in wherein U is substituted with a moiety selected from the group consisting of OH, NO, NO<sub>2</sub>, NH<sub>2</sub>, N<sub>3</sub>, halogen, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate, phosphoramidate, hydrazide, hydroxamate, hydroxamic acid, heteroaryloxy, aminoalkyl, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl and thioheteroaryl.
8. The compound of claim 1 in wherein X<sub>2</sub> is substituted with a moiety selected from the group consisting of OH, NO, NO<sub>2</sub>, NH<sub>2</sub>, N<sub>3</sub>, halogen, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate, phosphoramidate, hydrazide, hydroxamate and hydroxamic acid.
9. The compound of claim 1 wherein at least three of the groups R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are selected from -OX<sub>2</sub> or -N(T)Y;
10. The compound of claim 1 wherein R<sub>1</sub> is hydrogen.
11. The compound of claim 10 wherein independently at least one of R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, or R<sub>6</sub> is -N(T)Y, and at least one is -OX<sub>2</sub>.
12. The compound of claim 10 wherein independently at least two of R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, or R<sub>6</sub> are -OX<sub>2</sub>.
13. The compound of claim 10 wherein at least two of R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, or R<sub>6</sub> is -N(T)Y.

14. The compound of claim 1 wherein R1 is -N(Z)Y.
15. The compound of claim 14 wherein at least one of R2, R3, R4, or R6 is -N(T)Y.
- 5 16. The compound of claim 14 wherein at least two of R2, R3, R4, or R6 is -N(T)Y.
- 10 17. The compound of claim 14 wherein at least two of R2, R3, R4, or R6 are -OX2.
18. A method of synthesis of compounds of claim 10, wherein n is 1, comprising the step of reducing a synthetic intermediate of formula III, in which
- 15 V is bromine or chlorine,  
R6 and R7 are hydrogen, or together form a carbonyl oxygen,  
R5, R4, R3, and R2 are selected from the group consisting of OH, O-acyl, N<sub>3</sub>, NHDde, NHDTPM, NHZ, NHBOC, phthalimide, OX2, N(T)Y and an O-protecting group,
- 20 X2 is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,  
T is hydrogen or X2,  
Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(T)Y;

25

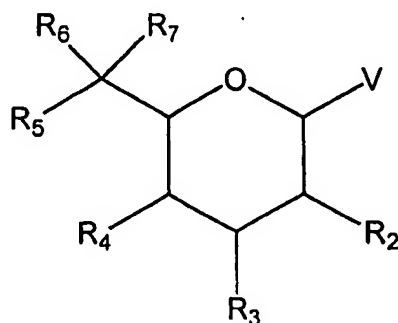


Z is selected from hydrogen or X1;

Q is selected from hydrogen or W;

- 5        The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

- 10       The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,



general formula III

- 15    19.    The method of claim 18, wherein R6 and R7 together form a carbonyl oxygen and R5 is O-alkyl, O-arylalkyl or O-aryl.
20.    The method of claim 19, wherein the R5 substituent is substituted

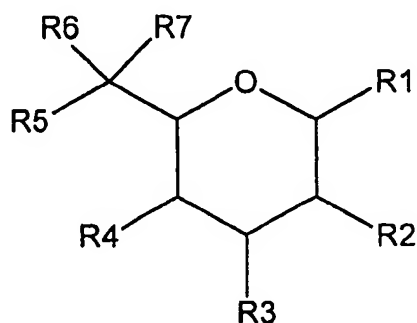
with a moiety selected from the group consisting of OH, NO, NO<sub>2</sub>, NH<sub>2</sub>, N<sub>3</sub>, halogen, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl,  
 5 carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate, phosphoramidate, hydrazide, hydroxamate, hydroxamic acid.

21. The method of claim 18, wherein the O- protecting groups comprise acetals and ketals which protect two adjacent oxygens.

10

22. A method of synthesis of compounds according to claim 14, in which n is 1, comprising the step of reacting a compound of formula III with an azide nucleophile, to form an anomeric azide and reduction of the anomeric azide to form an anomeric amine and reaction of the anomeric amine with an  
 15 electrophile.

23. A method of combinatorial synthesis of compounds of claim 1, wherein n is 1, comprising the step of immobilizing a compound of formula IV onto a support.



general formula IV

20

wherein

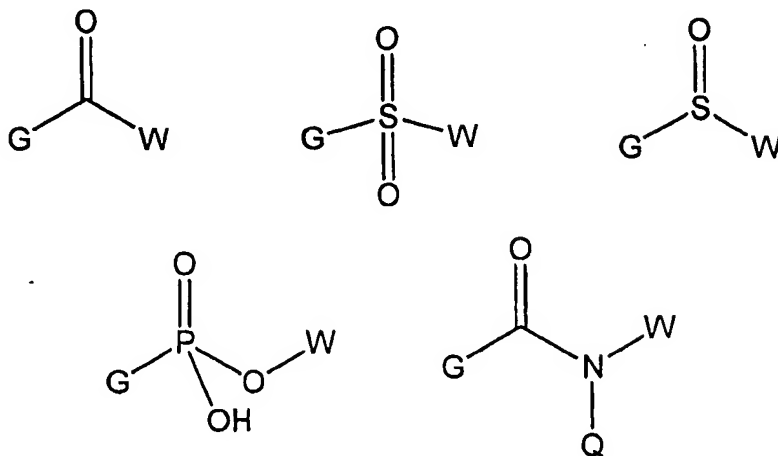
R6 and R7 are hydrogen, or together form a carbonyl oxygen;

R1 is selected from the group consisting of hydrogen; -N(Z)Y and -C(Z)Y

25 wherein;

When R1 is -N(Z)Y, then:

Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(Y)Z;



5

Z is selected from hydrogen or X1;

Q is selected from hydrogen or W;

The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

10

The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

15

When R1 is -C(Z)Y, then:

Y is selected from the group consisting of two hydrogen atoms, a double bonded oxygen (=O) to form a carbonyl, and a triple bonded nitrogen to form a nitrile,

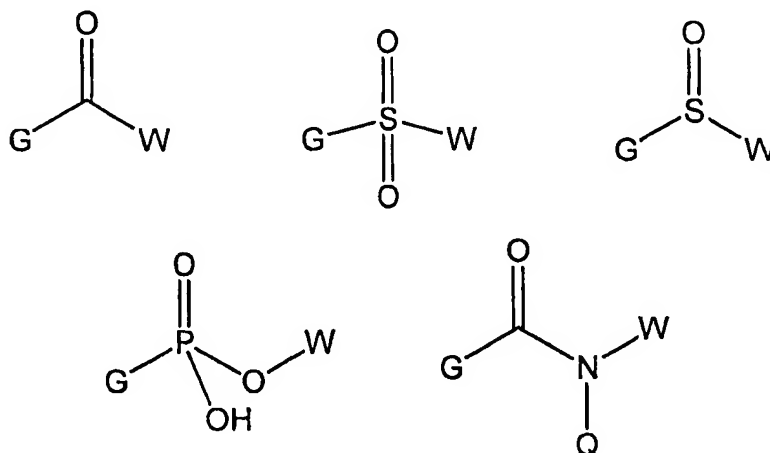
20

Z is absent, or is selected from hydrogen or U,

Wherein U is selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aminoalkyl, aminoaryl, aryloxy, alkoxy, heteroaryloxy, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

25

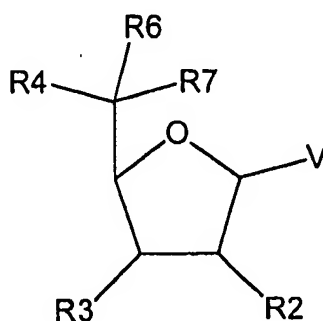
- R5, R4, R3, and R2 are selected from the group consisting of OH, O-acyl, N<sub>3</sub>, NHDde, NHDTPM, NHZ, NHBOC, phthalimide, OX<sub>2</sub>, N(T)Y and an O-protecting group, and the linkage between the compound of formula IV and
- 5 the support is through any one of positions R1, R2, R3, R4 or R5,
- X<sub>2</sub> is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,
- T is hydrogen or X<sub>2</sub>,
- Y is selected from hydrogen, or the following, where G denotes the point of
- 10 connection to the nitrogen atom in N(Y)Z;



- Z is selected from hydrogen or X<sub>1</sub>;
- 15 Q is selected from hydrogen or W;
- The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,
- 20 The groups X<sub>1</sub> are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,
24. The method of claim 23 wherein the support is selected from the
- 25 group consisting of derivatised polystyrene, tentagel, wang resin, MBHA

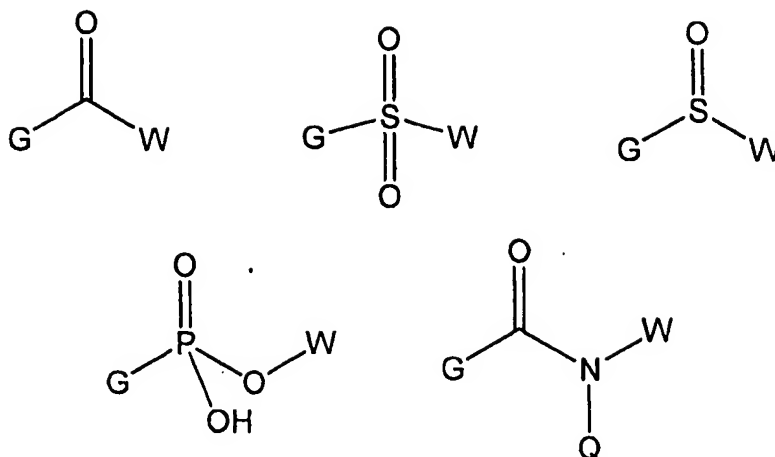
resin, aminomethylpolystyrene, rink amide resin DOX-mpeg, and polyethylene glycol.

25. A method of synthesis of compounds according to claim 13, in which  
 5 n is 0, comprising the step of reacting a compound of formula V in the  
 presence of a lewis acid with an azide source to form an anomeric azide,  
 reduction of the anomeric azide to form an anomeric amine and reaction of  
 the anomeric amine with an electrophile.



general formula V

- 10 in which V is -OAcyl,  
 R6 and R7 are hydrogen, or together form a carbonyl oxygen,  
 R4, R3, and R2 are selected from the group consisting of OH, O-acyl, N<sub>3</sub>,  
 15 NHDde, NHDTPM, NHZ, NHBOC, phthalimide, OX<sub>2</sub>, N(T)Y and O-protecting  
 group,  
 X<sub>2</sub> is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl,  
 heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,  
 T is hydrogen or X<sub>2</sub>,  
 20 Y is selected from hydrogen, or the following, where G denotes the point of  
 connection to the nitrogen atom in N(Y)Z;



Z is selected from hydrogen or X1;

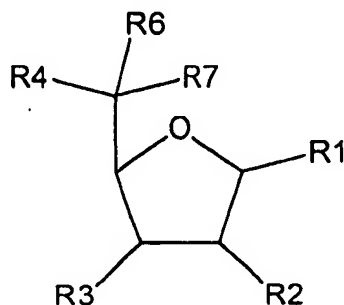
Q is selected from hydrogen or W;

- 5        The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

- The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl,  
 10        heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

26.        The method of claim 25, wherein R6 and R7 together form a carbonyl oxygen, and R4 is substituted O-alkyl, O-arylalkyl or O-aryl.

- 15        27.        A method of combinatorial synthesis of compounds of claim 1, wherein n is 0, comprising the step of immobilizing a compound of formula VI onto a support,



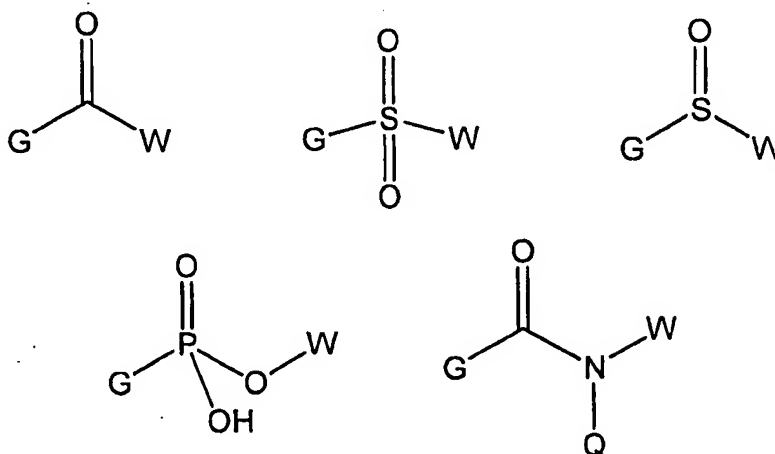
general formula VI



Wherein R1 is selected from the group consisting of hydrogen; -N(Z)Y and -C(Z)Y wherein;

When R1 is -N(Z)Y, then:

- 5 Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(Y)Z;



- 10 Z is selected from hydrogen or X1;

Q is selected from hydrogen or W;

The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

15

The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

- 20 When R1 is -C(Z)Y, then:

Y is selected from the group consisting of two hydrogen atoms, a double bonded oxygen (=O) to form a carbonyl, and a triple bonded nitrogen to form a nitrile,

- 25 Z is absent, or is selected from hydrogen or U,

Wherein U is selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aminoalkyl, aminoaryl, aryloxy, alkoxy, heteroaryloxy, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

5

R6 and R7 are hydrogen, or together form a carbonyl oxygen,

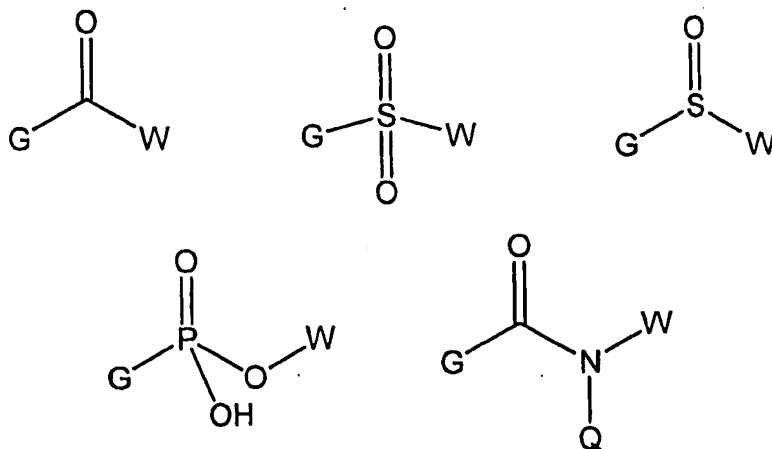
R4, R3, and R2 are selected from the group consisting of OH, O-acyl, N<sub>3</sub>, NHDde, NHDTPM, NHZ, NHBOC, phthalimide, OX2, N(T)Y and O-protecting group,

10 X2 is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,

T is hydrogen or X2,

Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(Y)Z;

15



Z is selected from hydrogen or X1;

Q is selected from hydrogen or W;

20 The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms ,

The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl,

25 heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

and the linkage between the compound of formula VI and the support is through any one of positions R1, R2, R3, or R4.

28. The method of claim 27, wherein the support is selected from the group consisting of derivatised polystyrene, tentagel, wang resin, MBHA resin, aminomethylpolystyrene, rink amide resin DOX-mpeg, and polyethylene glycol.

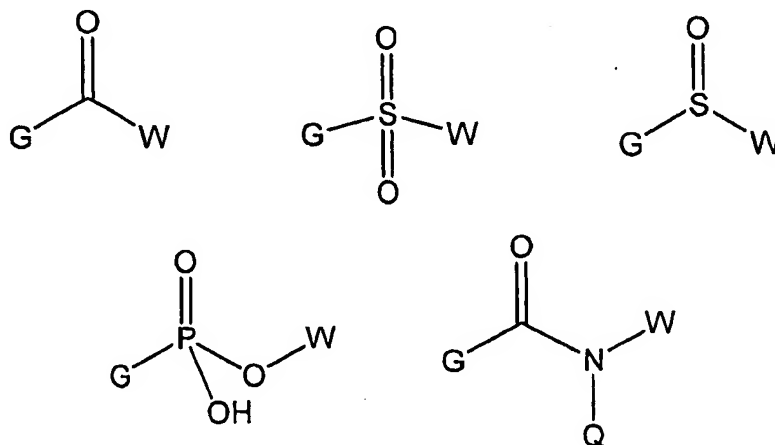
29. A method of solution phase combinatorial synthesis of compounds of claim 1, comprising the step of alkylating a free hydroxyl on a compound of formula IV or formula VI, wherein

R6 and R7 are hydrogen, or together form a carbonyl oxygen;

R1 is selected from the group consisting of hydrogen; -N(Z)Y and -C(Z)Y wherein;

15 When R1 is -N(Z)Y, then:

Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in N(Y)Z;



20

Z is selected from hydrogen or X1;

Q is selected from hydrogen or W;

The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

25

The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

5

When R1 is  $-C(Z)Y$ , then:

Y is selected from the group consisting of two hydrogen atoms, a double bonded oxygen ( $=O$ ) to form a carbonyl, and a triple bonded nitrogen to form a nitrile,

10

Z is absent, or is selected from hydrogen or U,

Wherein U is selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aminoalkyl, aminoaryl, aryloxy, alkoxy, heteroaryloxy, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

15

R5, R4, R3, and R2 are selected from the group consisting of OH, O-acyl,  $N_3$ , NHDde, NHDTPM, NHZ, NHBOC, phthalimide, OX2,  $N(T)Y$  and an O-protecting group,

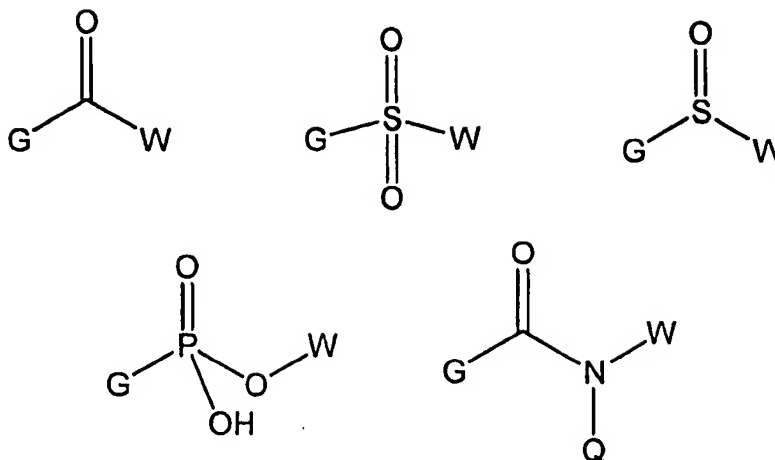
X2 is independently selected from alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl of 1 to 20 atoms,

20

T is hydrogen or X2,

Y is selected from hydrogen, or the following, where G denotes the point of connection to the nitrogen atom in  $N(Y)Z$ ;

25



Z is selected from hydrogen or X1;

Q is selected from hydrogen or W;

- 5        The groups W are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,

- 10       The groups X1 are independently selected from the group consisting of alkyl, alkenyl, alkynyl, heteroalkyl, acyl, arylacyl, heteroarylacyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl of 1 to 20 atoms,  
and any one of the protecting substituents may be removed prior to alkylation.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/AU03/00384

## A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. <sup>7</sup>: C07D 307/20, 307/22, 307/24, 309/08, 309/10, 309/14; C07H 5/04, 7/02, 7/04

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

ELECTRONIC DATABASES, SEE BELOW

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS Files: Medline, Biosis, WPIDS, CA. Keywords: saccharide, sugar, library, scaffold, amino acid, mimetic

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
|-----------|--|-----------------------|
| X         | S. A. W. GRUNER et al. Carbohydrate Based Mimetics in Drug Design: Sugar Amino Acids and Carbohydrate Scaffolds. Chem. Reviews. February 2002, 102, pages 491-514.<br>See whole document, and documents cited therein. | 1-29                  |
| P, X      | WO 02/32915 A1 (ALCHEMIA PTY LTD) 25 April 2002<br>See whole document, especially formulae Ib and Ic.  | 1-9, 14-26, 29        |
| P, X      | WO 02/32963 A1 (ALCHEMIA PTY LTD) 25 April 2002<br>See whole document, especially Examples 4, 5, 9 and 15  | 1-9, 14-26, 29        |

☒ Further documents are listed in the continuation of Box C

☒ See patent family annex

|   |  |
|---|--|
| * Special categories of cited documents:  |  |
| "A" Document defining the general state of the art which is not considered to be of particular relevance  | "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  |
| "E" earlier application or patent but published on or after the international filing date   | "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone   |
| "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| "O" document referring to an oral disclosure, use, exhibition or other means  | "&" document member of the same patent family  |
| "P" document published prior to the international filing date but later than the priority date claimed  |  |

Date of the actual completion of the international search  
12 June 2003

Date of mailing of the international search report  
20 JUN 2003

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU03/00384

| C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT |   |                       |
|---|---|-----------------------|
| Category*   | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
| X   | WO 98/08799 A1 (ALCHEMIA PTY LTD) 5 March 1998<br>See, for example, Figure 3.   | 1-9, 14-26, 29        |
| X   | SMITH et al. Synthesis of Oligomers of Tetrahydrofuran Amino Acids: Furanose Carbopeptides. Chem. Commun. 1998. Pages 2039-2040.<br>See compounds 4, 6, and 12. | 1, 2                  |

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU03/00384

**Box I** Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos :  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos : 1-29, in part  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  
The claims were considered too broad and too lacking in common technical features to allow a meaningful search of the claims as presently drafted, on economic grounds. The search was restricted according to the alleged inventive concept as communicated by the inventor, "a monosaccharide with  
Continued in Supplemental Box
3. ☐ Claims Nos :  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

**Box II** Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

There is no obvious "special technical feature" linking the compounds of the claims. Each individual compound claimed is therefore considered a separate invention.

The applicant has indicated that the intended special technical feature is "a monosaccharide with peptide mimetics attached." This feature is not explicitly represented in the present claims. This feature is also known in the art.

No invitation to pay additional fees was made.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.☐ No protest accompanied the payment of additional search fees.



# INTERNATIONAL SEARCH REPORT

International application No.

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## Supplemental Box

(To be used when the space in any of Boxes I to VIII is not sufficient)

### Continuation of Box No: I

peptide mimetics attached." Note that the search can not be considered to be complete with respect to the compounds claimed.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/AU03/00384

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

| Patent Document Cited in<br>Search Report |           | Patent Family Member |           |    |              |
|---|-----------|----------------------|-----------|----|--------------|
| WO  | 200232915 | AU                   | 200195282 |    |              |
| WO  | 200232963 | AU                   | 200195287 |    |              |
| WO  | 9808799   | AU                   | 38422/97  | CN | 1234790      |
|   |           | HU                   | 200000069 | US | 2003027925   |
|   |           |                      |           |    | END OF ANNEX |